Paying for New Drugs for New Bugs: Regulation is Only One Side of the Coin

FDA and Congress are making great strides in improving the regulatory pathway and intellectual property protection for anti-infectives. But without changes in the reimbursement process, the package of incentives may not be enough to spur innovation in the class.

Deadly infections with bacteria that resist even the strongest antibiotics are on the rise in hospitals in the United States, and there is only a “limited window of opportunity” to halt their spread, health officials at the Centers for Disease Control & Prevention warned this spring. In this case, the bacteria in question were bugs normally found in the gut.

According to the CDC, they have acquired a lethal trait: they are unscathed by antibiotics, including carbapenems, a group of drugs that are generally considered a last resort. When these resistant germs invade parts of the body where they do not belong, like the bloodstream, lungs or urinary tract, the illness may be untreatable. It was one of these bugs – a drug-resistant form of the feared bacteria Klebsiella – that triggered a notorious outbreak in 2011 at a hospital at the National Institutes of Health that killed six people and made another 11 seriously ill.

In the report, CDC Director Dr. Thomas R. Frieden called these and similar bugs “nightmare bacteria” and noted that they could pass their trait for drug resistance — encoded in a scrap of genetic material called a plasmid — along to other bacteria.

Aware of these threats, Congressional and Administration officials are fashioning a number of new initiatives to accelerate the development of a new generation of more potent anti-infectives. Principal among these new policy efforts was the Generating Antibiotic Incentives Now (GAIN) Act that took effect October last year. Another recent proposal aims to address how FDA regulates these drugs.

However, these reforms which incentivize the development of new anti-infectives need to go hand-in-hand with changes in the way that they are covered if we are going to provide proper incentives for these endeavors and achieve the singular goal: a new generation of better drugs.

The GAIN Act seeks to create incentives to encourage the development of products to treat, prevent, detect and diagnose antibiotic-resistant infections by streamlining regulation and extending the length of time an approved drug is free from competition. Annually, tens of thousands of Americans die from
infections, largely acquired in hospitals that are resistant to antibiotics. So under the new law, anti-infectives targeted to dangerous, resistant pathogens (dubbed Qualified Infectious Disease Products under the GAIN Act) will receive 5 years of market exclusivity in addition to the standard 5 years of exclusivity for a new chemical entity under Hatch Waxman, for a total of 10 years of market exclusivity. (That exclusivity runs concurrent with patent protection, if any).

The provision can offset the cost of developing older molecules into new anti-infective drugs, where most of the intellectual property around the drug’s molecular “composition of matter” has already lapsed. But the fact is that most completely novel agents, of the sort we need, will already have more than 10 years of protection to burn down. The never-before-discovered molecules will largely be unaffected by the new law.

More recently, President Obama’s Council of Advisors on Science and Technology (PCAST) took up a Food and Drug Administration idea for the creation of an alternative approval pathway for certain drugs targeted to address unmet medical needs, referred to as Special Medical Use (SMU). Under the proposed pathway (which FDA plans to narrowly apply to anti-infectives targeted to resistant pathogens) FDA would accelerate the development of novel agents based on more preliminary clinical data in exchange for authorities that would give the agency more direct control to regulate use of the resulting product to make sure it is only prescribed in settings where FDA approves.

Getting the regulation and intellectual property right are just two elements of the challenge. Alone, they will not get the job done. We also need to put in place new coverage and payment policies that will properly reimburse anti-infectives that are targeted to narrow, resistant bugs and may be held in reserve as a result – with their use restricted for public health reasons. We need to address the incentive side of the equation, especially if streamlined development is going to go hand and hand with ideas like the Special Medical Use to restrict use that will ultimately narrow markets, and constrain sales.

Most of the ideas proposed have focused on the intellectual property afforded new agents, and the patent terms. Few have directly addressed payment. That needs to change if we are going to usher in a new complement of better drugs for bad bugs.

A novel pathway created over a decade ago by Congress - the new technology add-on payment (NTAP) - may provide a foundation for new policies that seek to bridge initiatives aimed at underwriting the development of new drugs, with schemes aimed at rewarding them in the marketplace and making sure patients are able to get access to these medicines.

**The History of the New Technology Add-on Payments**

Introduced in 2001, the NTAP program is designed to support timely access of innovative therapies to treat Medicare beneficiaries in the inpatient setting. The program is only available to new technologies. It is designed to help offset structural obstacles in current Medicare reimbursement policies that can sometimes put beneficial new technologies at a pricing disadvantage, discouraging their use – especially when it comes to drugs aimed at hospital-based problems.

This is precisely where most serious infections get their start—or at the least, end up presenting and being treated.

Under Medicare’s Inpatient Prospective Payment System, Medicare pays hospitals a fixed, prospectively determined amount of money for each inpatient hospitalization. These payments are based on Medicare severity diagnosis-related groups. Each MS-DRG has a payment weight assigned to it, based on the relative amount of resources used to treat Medicare patients for a particular medical problem.

These fixed payments are intended to encourage hospitals to operate efficiently. They also help control overall costs to the Medicare program. But the payment system also puts hospitals at risk for higher costs associated with changes in technology, since new innovations can be introduced without adjustments to payment levels.

Although CMS annually revises these fixed payments using data from actual inpatient claims submitted to the agency, the MS-DRG classifications and weights are generally based on historical data from claims for inpatient services that can be as much as two years old. This can create a two- to three-year delay between the market introduction of a new technology and the recalibration of MS-DRG weights to reflect its added cost.

During this period, hospitals that adopt a new technology may lose money for using it. This creates a significant and pervasive disincentive for the adoption of new technologies, sometimes even those that might help to achieve quality and outcome improvements and offset longer-term costs to Medicare. When hospitals choose to use newer, perhaps better, but also more expensive new technologies, they may lose money.

In 2000, Congress took steps to address these concerns. Section 533 of the Medicare, Medicaid, and State Children's Health Insurance Program Benefits Improvement and Protection Act of 2000 created NTAP to serve as an additional payment that “recognize[s] the costs of new medical services and technologies under the [inpatient] payment system.”

The goal was to bridge that 2- to 3-year recalibration delay, to help offset some
of the financial losses that a hospital could incur by using a beneficial new technology.

These add-on payments are provided for the initial years after a new technology is first introduced. It covers the period of time required for CMS to accumulate enough inpatient claims data for MS-DRG rate setting to more accurately reflect the added costs of the new product. In 2001, CMS issued regulations specifying the criteria for granting NTAPs and determining the amount of the payments.

For technologies that meet the eligibility criteria and receive CMS approval, the determination of the NTAP amount is based on the cost to hospitals for the new technology. The payments are made only when the estimated cost of a case exceeds the payment that would otherwise be made to the hospital. The NTAP amount is equal to the lesser of 50% of the amount by which the total covered costs of the case exceed the MS-DRG payment when the new technology is adopted by providers, or 50% of the cost of the new technology.

The end goal: These payments are meant to provide a partial offset to the cost of using the new technology when the individual patient cases are more costly than the historical amount paid under the existing DRG.

Case Study: Expanding on a Good Policy

Optimer Pharmaceuticals Inc. recently received NTAP approval for its product Dificid (fidaxomicin) tablets, starting in the 2013 fiscal year. Dificid is an oral medication indicated for the treatment of Clostridium difficile-associated diarrhea (CDAD) in adults 18 years of age and older. This decision was unique in that only one prior drug had received NTAP status (Eli Lilly & Co.’s now withdrawn sepsis treatment Xigris) and no orally administered treatments had received an NTAP designation previously.

Dificid represents a novel treatment for CDAD, the most common symptom of C. difficile infection, currently one of the most frequently occurring healthcare-associated infections among Medicare beneficiaries. In its application for an NTAP, Optimer Pharmaceuticals highlighted clinical evidence to demonstrate “substantial clinical improvement” over existing therapies. In Phase III clinical trials, Dificid achieved comparable initial clinical response versus vancomycin and superior sustained clinical response versus vancomycin – meaning a higher proportion of patients achieve clinical response and remain free of CDAD recurrences through 25 days after the end of treatment.

Based on this data, CMS agreed to grant an NTAP to Dificid, and also observed that the drug has the potential to reduce hospitalizations and physician office visits as well as the recurrence of CDAD.

While the NTAP pathway has been in place for many years, it has been seldom used for pharmacologic agents. Typically, these add-on payments were granted to medical devices on procedure-based technologies. Optimer’s receipt of the NTAP marked the only instance in which CMS has granted the add-on payment to an oral medication in the 10-year history of the program. Under CMS’ previous policy, oral medications were deemed ineligible for NTAP because they do not involve procedures designated by ICD-9-CM codes.

To accommodate Dificid in the NTAP program, CMS revised its policy to allow the use of National Drug Codes to identify oral drugs. CMS’ ultimate flexibility in recognizing an oral medication such as Dificid for an NTAP aligns with the high burden of illness caused by CDAD, the significant morbidity and mortality caused by this condition in the Medicare population in particular, and the high rates of costly recurrence of this condition in the hospitalized setting.

This experience underscores the unique role that the NTAP and other similar policies may have in driving investment in better drugs for bugs – and other areas that are high priority for quality improvement and cost reduction for the Medicare program.

- First, the NTAP can be used to provide an additional, powerful incentive for innovators to invest in the development of drugs aimed at vexing bugs. Regulatory reform alone is not enough. Patent reform is not a sufficient incentive either if payment cannot be put into place. There has to be a path to better access. NTAP provides a vehicle for policymakers to use reimbursement as a tool to support investment in technologies that help achieve more value to beneficiaries.

- Second, this type of policy can directly support public health goals already being pursued by CMS. In this instance, the agency used the payment for a product that supported its efforts to reduce hospital-acquired infections.

- Finally, broadening the use of NTAP for a wider range of technologies can help offset structural impediments to the development of new technologies that can deliver better overall value to the Medicare program.

Lessons Learned

The Dificid case study provides some useful lessons on how the NTAP can be expanded to create more incentives for high-value innovations that combat worrisome infections – especially those that have their origins, or conclusion, in the hospital.

There are steps policymakers can take to make NTAP a more potent tool in the present fight.
To grant Dificid an NTAP, CMS revised its policy to accommodate the approval of an orally administered technology using a new coding approach. Existing guidelines outlining how a new technology can qualify for an NTAP are also too formulaic. They focus on explicit calculations around cost of care with new technologies as opposed to implicit considerations of value. Only technologies that meet specific cost thresholds and demonstrate “substantial clinical improvement” over existing products can qualify.

This guidance should be revisited. For example, in its current form, the existing guidance on NTAP does not incorporate current policy goals that have become a more prominent part of Medicare’s efforts to reform payment. CMS should take this opportunity to revise the criteria for granting NTAP, using its considerable leverage over payment to create incentives for the development of new technologies that enable CMS to achieve its public health objectives and get more value for beneficiaries.

For Optimer, the NTAP will help defray the cost of using Dificid so that hospitals receiving fixed DRG reimbursement do not face a disincentive from prescribing the agent. In fiscal year 2013, CMS will pay hospitals an additional amount up to $868 for cases involving Dificid when the costs of the case exceed the MS-DRG payment amount. While Optimer believes the product will deliver superior patient outcomes that justify its costs, the NTAP payment provides a very explicit offset to the product’s costs, creating incentives for its appropriate, FDA-approved use.

Historically, CMS has not used the NTAP policy in this way. These payments have previously been adopted sparingly, and mainly in the context of medical devices. We believe this use of the NTAP warrants more consideration. The program could provide the foundation for new Medicare policies aimed at rewarding innovations that deliver high value to patients while supporting broader quality initiatives being pursued by the agency.

CMS should revisit the regulations governing NTAP to incorporate clearer incentives for products that help the agency achieve its broader public health goals. CMS should move away from its formulaic approach for defining when a product would qualify for an NTAP. The agency should establish broader criteria that incorporate adjustments for products that help to achieve quality goals. If the criteria for qualifying for an NTAP were more explicitly tied to the kinds of product attributes that helped CMS achieve other public health goals, the inducements could inform the financial considerations made when selecting programs for further development.

The experience of Dificid frames a path for how CMS could better align private capital behind these public health efforts to achieve more investment and innovation targeted against vexing bugs, more value for the Medicare program, and more opportunities to advance the public health of its beneficiaries.

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