



A Fever in the Drug Industry

The unique nature of antibiotics means that some see a need for higher prices

By ANDREW SIDDONS

Even as lawmakers debate policies to lower drug prices and curtail Big Pharma profits, manufacturers that specialize in new antibiotics are begging Congress for help in staying afloat.

Investors don't see the same money-making potential in antibiotics as with cancer and other chronic disease drugs. That's despite a clear public health need for new antibiotics, since many don't work as well due to years of overuse.

A bill (S 1712) before Congress aims to help by boosting Medicare payments for the products. Antibiotic manufacturers and health experts view it as a necessary change to help keep the market afloat.

Like previous laws Congress enacted to encourage antibiotic development, supporters view it as a short-term solution and say more significant changes will be necessary.

But a bill that could encourage the use of more expensive drugs, even if it is well-intentioned, will likely struggle in a Congress focused on lowering drug costs, despite the consistent alarm bells from industry and public health experts.

The situation for the antibiotics industry is only getting more challenging, according to Amanda Jezek, senior vice president of public policy and government relations at

the Infectious Diseases Society of America, a professional group for doctors and scientists. She cited the bankruptcy earlier this year of antibiotic developer Achaogen, even though the company won approval for a new product less than a year earlier.

"There definitely needs to be government action to stabilize the market to prevent the few remaining companies from going bankrupt," she says. "The impor-

Courtesy Mary Millard



NEAR DEATH EXPERIENCE: Millard survived sepsis thanks to an antibiotic drug, but there are side effects.

tance of antibiotics to the very foundation of modern medicine would argue that if the government has been willing to intervene on behalf of other industries, how could we not do that for antibiotics?”

Bacteria that are resistant to antibiotics treatment are responsible for 2 million infections and 23,000 deaths each year, according to the Centers for Disease Control and Prevention.

Mary Millard, a 60-year-old former nurse, was in the hospital in 2014 for surgery after an aneurysm and a heart valve problem. Before the surgery, she had a heart attack. The procedure used to keep her heart beating led to a *Pseudomonas aeruginosa* infection.

This particular bug causes around 6,700 drug-resistant infections and 440 deaths per year, according to the CDC, which considers it one of the top 18 threats among resistant bacteria.

Millard survived her immune system’s extreme response to the infection, an often-deadly condition known as sepsis. She needed another surgery to clear up the infection, but the bug couldn’t be completely killed off and persists around the areas where she needed surgery. To keep the bacteria from spreading further throughout her body and prevent another instance of sepsis, she needs a daily dose of the common and inexpensive antibiotic ciprofloxacin, which has side effects like tendonitis and joint pain.

“It’s supposed to be for life unless they

come up with something else,” she says.

Because the antibiotic she’s on also kills off the good bacteria that normally exists in healthy individuals, her risk of contracting other infections is also much higher than the average person, she says. As a result, she no longer works, though she does speak at conferences and to medical industry groups about her five-year struggle.

“I can be hospitalized at any time. I have multiple doctors’ appointments every month,” Millard says. “It’s kind of crazy, and I really, really had to get used to a new normal living with the infection.”

Industry Challenges

A combination of unfavorable reimbursements, scientific issues that make clinical trials challenging, and the need to prescribe any particular drug as infrequently as possible make it difficult to sustain antibiotic research programs, say advocates. That’s true even though Congress enacted two laws in the past decade to bolster development.

It can cost more than \$150 million and take up to a decade to test a new antibiotic before going through Food and Drug Administration approval, according to one estimate. Once antibiotics are on the market, they are less profitable than some other drugs. One product that is more effective against resistant bacteria — the type of drug lawmakers want to encourage — produced about \$130 million per year, according to the

Pew Charitable Trusts, which runs a project on antibiotic resistance. By comparison, Pew found, at least 20 cancer drugs had sales of \$1 billion or more in revenue — highlighting why investors might be more drawn to other disease areas over antibiotics.

Achaogen, the bankrupt company, won FDA approval in June 2018 for a drug to treat urinary tract infections caused by so-called “nightmare” bacteria that is difficult or impossible to treat with more commonly used antibiotics. Less than a year later, in April 2019, the company filed for bankruptcy and illustrated why some of the current government incentives for antibiotic development might not go far enough.

The drug, Zemdri, was designated a “qualified infectious disease product” for certain uses. That designation was part of a 2012 FDA reauthorization law (PL 112-144) that was intended to help the problems that are still plaguing the industry.

The law gave new antibiotics that treat “serious or life-threatening infections” an extra five years of exclusive sales on top of other monopoly periods they would normally receive. Those products also receive an expedited FDA review process, meaning companies might start being able to sell the drug more quickly than they otherwise would. The product was also eligible for a higher-than-average Medicare payment designed to encourage the uptake of new technologies.

Greg Frank, director of infectious disease policy at the drug industry trade group Biotechnology Innovation Organization, says the 2012 law, known as the Generating Antibiotic Incentives Now, or GAIN Act, was necessary but not sufficient.

“Many companies would not be here if it wasn’t for the GAIN Act,” says Frank, who leads a coalition of drug companies, scientists and policy experts called “Working to Fight AMR,” or antimicrobial resistance. “But what we found was, of course, it did not solve the problem. It only delayed the sort of ‘valley of death’ for companies.”

Similarly, in 2016, as part of a wide-ranging medical research law (PL 114-255), Congress created a new FDA approval pathway for antibiotics meant to serve limited patient populations. It’s supposed to make it easier for companies to conduct studies with smaller

meeting that the pathway is “only one part of the ecosystem fix,” and that the drugs are “not to be used for the ordinary circumstance.”

Bill to Boost Payments

Now policymakers are focusing on a different kind of incentive. Rather than keeping development costs down, or extending a monopoly period, some policymakers are saying that these are drugs worth paying more for, despite the broader effort to lower drug prices.

“The paradox of antibiotics is that they’re essential to underpinning medicine,” yet they don’t command high prices, says Allan Coukell, senior director of health programs at the Pew Charitable Trusts.

“We rely on their ability to do intensive care medicine, transplants, oncology, all of those things,” he says.

that by paying the drug’s average price plus a slight markup.

The bill would also require hospitals to have antibiotic stewardship programs in place in order to obtain the higher reimbursement for new products. Stewardship programs are meant to ensure that the appropriate antibiotics are used in the proper context. Recently, the Trump administration put in place a rule that requires hospitals to have stewardship programs in place in order to qualify for Medicare and Medicaid reimbursement. It’s the first time the policies will be required at a federal level by hospitals, though congressional action would be needed to codify such a policy.

Stewardship policies also point to the fundamental tension with investing in new antibiotics: They need to be used as sparingly as possible to maintain their effectiveness.

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— Amanda Jezek, *Infectious Diseases Society of America*

numbers of patients and the companies only have to show that a drug is simply “non-inferior” to an existing treatment, instead of offering an improvement over the standard of care. The logic behind the different standard is that having multiple products that work just as well is a better option when drug resistance is a risk.

So far, companies have only taken advantage of the process for two drugs. The FDA is still finalizing guidance on how companies can take advantage of the new pathway.

At a public meeting on the guidance this summer, drug industry representatives suggested that companies were looking for more certainty on which products would qualify under it. And while the pathway can help with one hurdle for new products, the products that use it will still be meant for use in limited populations — and could have a lower return-on-investment potential.

John Rex, chief medical officer at antifungal drug company F2G, noted at the July FDA

Medicare’s reimbursement system is one reason that it’s tough to charge enough for antibiotics.

Some of the worst infections occur in hospital settings, and antibiotics are often a key ingredient in many other procedures. But Medicare doesn’t always reimburse for every single part of treatment, in an effort to keep costs down. Instead, it pays fixed amounts based on the condition that is being treated, which provides an incentive for doctors and hospitals to come up with the most cost-effective solution.

To encourage the use of new products, Medicare pays hospitals extra — but that still just means 50 percent of the actual cost to the provider. It recently announced that it would pay more — 75 percent — for antibiotics designated with the “qualified infectious disease product” status. The bill before Congress, by Sens. Johnny Isakson, a Georgia Republican, and Bob Casey, a Pennsylvania Democrat, would have Medicare provide more than

“Right now, there is no prospect of getting sufficient return for a lot of these products just through sales to make this a viable business,” says Coukell.

The bill “buys us time,” says Frank.

But he and others say more should be done.

One proposed solution involves the government awarding prize money to drug companies who develop new antibiotics so that they can recoup their investments and worry less about future sales. Some have suggested a kind of subscription model, where hospitals pay for the ability to access a drug when it is really needed, rather than for each individual dose.

“There’s no silver bullet here that totally transforms this — so we need a bunch of policies working together,” Coukell says. If policymakers don’t figure out how to address this soon, he says, market forces might be spurred by an outcome that no one wants to see.

“We’ll have lots of people dying of resistant infections and the prices will rise,” he says. ■