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PRICING POLITICS

BY STEVE USDIN, WASHINGTON EDITOR

Presidential candidates from both parties are tapping into public anger over prescription drug prices and responding by repeating old proposals, like controlling prices or lowering FDA approval standards, that won't be enacted and probably wouldn't work if they were put into practice.

Out of the limelight and far from the political pontification, the renewed attention to drug prices is stimulating quieter discussions about new approaches to drug spending that might benefit patients, the healthcare system and developers of innovative medicines.

These include efforts to increase the transparency of drug prices, and, taking a cue from the private sector, proposals to reward innovation and reduce spending on lower-value products.

Patient groups and drug companies are also pushing for policies that would change health insurance plan designs in ways that would increase access to medicines by reducing out-of-pocket costs.

It will take time, and a calmer political environment, for new ideas to gain traction in Congress and at HHS. In the meantime, industry lobbyists, trade associations and pundits are gearing up for yet another round of vituperative drug pricing debates.

With the possible exception of acting to increase competition for off-patent drugs serving very small populations, the stalemated 114th Congress will not translate Americans' anger over drug prices into legislation (see "Unrealistic Prescriptions," page 3).

The Obama White House has also run out of viable options for affecting drug prices.

The lack of immediate action in Washington does not mean that public perceptions of pharmaceutical profiteering are irrelevant, even in the short term.

The corrosive political environment has eroded congressional support for creating new incentives for

Left to right: Democratic Reps. Lloyd Doggett (Texas), Marcy Kaptur (Ohio), Elijah Cummings (Md.), Jim McDermott (Wash.) and Jan Schakowsky (Ill.)

developing drugs to meet public health needs, allowed CMS to implement a reference pricing scheme for biosimilars, and fertilized proposals to expand NIH's and FDA's missions to include cost containment (see "Compounding Prices," page 6).

Inaction in Washington is also prompting efforts to mandate drug price controls at the state level (see "Laboratories of Democracy," page 4).

MOVING TO VALUE

Mark McClellan, who served as FDA commissioner and CMS administrator in the George W. Bush administration, thinks there is an appetite in Washington for moving past the old arguments between supporters of price controls and those who say that unfettered pricing freedom is needed to support innovation.

The discussion is moving toward determining how to "integrate drugs into the big shift in healthcare to accountability payment models based on results," he told BioCentury. McClellan is director of the Duke-Robert J. Margolis, MD, Center for Health Policy at Duke University. He also serves on the board of Johnson & Johnson.

"It has been challenging and certainly not straightforward to implement those kinds of models for doctors and hospitals, and it won't be easy for drugs," McClellan said. "That doesn't mean it won't happen."

"There is a significant willingness in the drug industry to explore and try to implement these kinds of models," he added. He cited experiments with outcomes-based contracts.

McClellan pointed to Medicare Part B drug payments as a potential target for change.

The current system of paying physicians who administer drugs in outpatient settings the average sales price (ASP) plus 6% "is not tied to value in any meaningful way," he said.

One potential solution is to replace the Part B reimbursement system with something like Part D, McClellan said. Under Part D, private plans compete to offer drug benefits within broad parameters established by CMS. Plans use formularies to obtain discounts on drugs, and compete on the basis of drugs covered. They can use co-pays and other design characteristics to favor high-value and discourage utilization of lower-value drugs.

"We used to think that for very specialized drugs there is only one treatment for a patient, so you can't create a formulary model to create competition. That is not so true anymore," he said.

Value-based pricing models, which encompass a range of concepts that tie price to value, such as outcomes- and indication-based pricing, could align economic incentives with public health priorities, but McClellan noted they are not a magic bullet: "Just moving to value-based pricing won't solve the rise in spending."

This is one of the lessons from the new generation of HCV treatments, which, because of the large number of potential patients, would have caused economic waves even if they had been priced lower. "Even though by most economic models the drugs were worthwhile" they had a huge impact on the growth of drug spending in 2014 that translated into an increase in the overall cost of healthcare, McClellan noted.

The best way to create economic space for innovation, including new drugs, is to speed efforts to make the entire healthcare system more efficient, McClellan said. He pointed to the creation of accountable care

organizations and advancing digital and telemedicine as steps that could create space for increased spending on drugs.

BARRIERS

Legislation might be needed to overcome barriers to value-based drug pricing models.

Regulatory barriers to value-based pricing of drugs — both real and perceived — were on display at a forum on pharmaceutical pricing that HHS convened in November.

Christi Shaw, U.S. country head at Novartis AG, and Kenneth Frazier, chairman and CEO of Merck & Co. Inc., said FDA's prohibition on discussion of off-label uses of drugs is a barrier to outcomes-based pricing contracts.

"When you run a clinical trial and get approval, what is on the label has to be the basis for outcomes contracts," Shaw said. For example, she said, if a payer wants to look at total hospitalization and that is not on the label, it can't be included in an outcomes-based contract.

Frazier, who also is chair of PhRMA, added, "In order to have a good sense of what the true real-world risks are, we sometimes have to look beyond what's on the label of the drug. We are restricted from communicating about that by FDA."

However, according to Coleen Klasmeier, a partner at Sidley Austin LLP and former FDA attorney, it isn't clear whether such communications are actually illegal, and ambiguity can deter companies from taking steps that are legal.

"The current enforcement climate and ongoing regulatory uncertainty makes it hard to determine in advance whether a particular activity is on the right side of the line," Klasmeier told BioCentury. "Even if you have a sound legal risk assessment that's supportive, you're stuck with the risk of an aggressive prosecutor taking a different view. Indeed, there's so much about the current paradigm that's subject to debate that the prosecutors themselves don't always have a good mastery of the relevant legal principles."

FDA is working to clarify the issue, agency spokesperson Sarah Peddicord told BioCentury in an email.

"The Agency is currently examining its rules and policies relating to manufacturer communications regarding approved drugs, including communications of unapproved use information and dissemination of healthcare economic information to formulary committees and similar entities," she said. "The purpose of this review is to help ensure that our implementation of FDA's legal authorities best protects and promotes the public health in view of ongoing developments in science and technology, medicine, health care delivery, and constitutional law. The Agency continues to be actively engaged in this effort and intends to issue new guidance and solicit public input in the near future."

According to Shaw, FDA regulations also prevent companies from working with payers to develop creative payment strategies prior to approval. She cited the example of chimeric antigen receptor T cell therapies Novartis is developing to treat chronic lymphocytic leukemia (CLL).

Novartis has achieved dramatic cures of CLL patients, Shaw said, adding, "How do you charge for that?" She warned that CAR T therapies may create a "Sovaldi situation" because "we can't talk to payers before approval."

UNREALISTIC PRESCRIPTIONS

Affordability of prescription drugs is the most important healthcare issue for Americans according to a national survey the Henry J. Kaiser Family Foundation released in October. A total of 77% of those surveyed put drug prices on the top of their healthcare priority list, and 63% -- including 56% of Republicans -- agreed "government action to lower prescription drug prices" should be the top priority for the president and Congress.

Politicians are acutely aware of the polling data.

Hillary Clinton's campaign has been running a television advertisement in Iowa ahead of the caucuses that claims, inaccurately, that "in the last seven years drug prices have doubled." In fact, since more than 80% of prescriptions in the U.S. are generics, overall prices haven't changed much.

The ad also asserts, "Hillary's going to take on the drug companies," and says she plans to "require Medicare to negotiate lower drug prices, let people buy their prescription drugs from countries like Canada at half the price, and cap monthly prescription drug costs for every American."

The ad concludes with Clinton standing in front of a pharmacy counter saying, "The drug companies have been overcharging for long enough. It's time to fight back."

Bernie Sanders is more bellicose in his denunciation of drug companies, but his proposals are similar to Clinton's.

Both Sanders and Clinton have been around long enough to know that their drug price control proposals have been attempted numerous times over the past 15 years, and they failed to pass Congress even when Democrats had a much stronger position than they will have in 2017.

Regardless of who wins the White House in November, there is little chance that HHS will be given power to "negotiate" -- a euphemism for "set" -- Medicare drug prices.

All of the Republican presidential candidates have said they would take steps to lower prescription drug prices.

In a video of remarks at a private campaign event in October, Florida Sen. Marco Rubio said pharmaceutical companies engage in "pure profiteering" when they increase prices to offset declining volumes of prescriptions.

Rubio, Sen. Ted Cruz of Texas, N.J. Gov. Chris Christie and Jeb Bush have all pointed fingers at FDA, asserting that drug development could be made dramatically quicker, resulting in lower prices. They offer no evidence, however, of a correlation between FDA review times and drug prices. In any case, Congress isn't likely to change drug approval standards anytime soon.

— STEVE USDIN

PhRMA is trying to get provisions lifting restrictions on drug company communications with health plans incorporated into the Senate counterpart for the House 21st Century Cures Act.

Democrats in Congress have been reluctant to loosen restrictions on drug company communications, and as an alternative to legislation, the trade association is also actively looking for disputes that could form the basis for First Amendment litigation.

SCHADENFREUDE

International news coverage that has made Martin Shkreli, the former CEO of Turing Pharmaceuticals AG, the world's best-known ex-pharmaceutical company executive has also prompted Republicans to overcome their reluctance to discuss drug pricing. The leading Republican presidential candidates have taken verbal swipes at Shkreli.

Bowing to pressure from Rep. Elijah Cummings (D-Md.), the ranking Democrat on the House Oversight and Government Reform Committee and leader of the Affordable Drug Pricing Task Force, committee Chairman Jason Chaffetz (R-Utah) has scheduled a Jan. 26 hearing on drug prices.

There is bipartisan support for helping clear the massive backlog of FDA generic drug reviews, and for government proactively identifying and speeding ANDAs for essential off-patent drugs that could be hijacked by companies seeking to emulate Turing's business model.

Developers of innovative drugs are enjoying a bit of schadenfreude over the public lashing that Turing and drug companies like Valeant Pharmaceuticals International Inc. that have pursued research-free business models are experiencing.

It hasn't taken long, however, for the media and politicians to move from criticizing exorbitant prices of small-market generics to scrutinizing routine increases in the prices of new drugs that far exceed inflation.

In the U.S., average wholesale price (AWP) often goes up even as competitors enter the market.

The National Drug Index compiled by pharma data services company Truveris Inc. also shows consistent price increases, even in crowded therapeutic classes. The NDI is an index of U.S. average prescription drug prices that includes discounts and rebates.

From December 2014 to December 2015, Truveris showed rheumatoid arthritis (RA) drug prices net of discounts and rebates increased 17%, while multiple sclerosis (MS) drugs increased 11%.

Overall, brand drug prices increased about 15% over the same period, far more than the 4% increase in generic drug prices, Truveris reported.

The Obama administration has tried to take on drug prices, for example by including requests for Medicare drug negotiation authority and shorter biologics exclusivity provisions in budget requests.

PhRMA, BIO and drug companies have shut down these attempts, and there is no evidence that the next administration would have more success in convincing Congress to adopt drug price controls.

PRICING TRANSPARENCY

The White House has also learned that any attempt to unilaterally cut drug spending will be fiercely resisted.

In 2014, CMS announced plans to eliminate two of the six protected classes for which Medicare Part D plans must provide "substantially all" approved drugs. The political blowback from patients who feared they would lose access to medicines forced the agency to backtrack.

CMS lacks the political clout to attack price increases head-on, so it has decided to build support for action by shining a light on pricing practices.

In December, CMS released a "dashboard" of information about Medicare spending on prescription drugs. The dashboard includes spending and utilization data for 40 Part D and 40 Part B drugs; it does not reflect rebates or other price concessions.

Andy Slavitt, acting CMS administrator, acknowledged limitations to the data in a blog posting, including the lack of data on discounts and rebates or information about the medical benefits of specific drugs. "We realize the dashboard doesn't provide a complete picture, but still believe that, by sharing this information and allowing people to analyze the data, we can increase the knowledge around drug spending and support efforts that are evaluating whether public dollars are being spent most effectively," he wrote.

LABORATORIES OF DEMOCRACY

Having failed to make a dent in Washington, drug price control advocates are turning to the states, especially those that make it relatively easy to place initiatives on ballots.

The AIDS Healthcare Foundation (AHF), which has led campaigns seeking government intervention to reduce the prices of several drugs, has succeeded in placing a drug pricing initiative before California voters in the November election.

The California Drug Price Relief Act ballot initiative accuses pharmaceutical companies of "charging inflated drug prices," " lavishing excessive pay on their executives," and imposing "an unnecessary burden on California taxpayers that ultimately results in cuts to health care services and providers for people in need."

The initiative prohibits the State of California from paying net drug prices that are higher than those paid by the U.S. Department of Veterans Affairs. The VA has a restrictive formulary, and drug companies are legally required to provide the VA deep discounts. The VA pays about 20% less for drugs than other government programs.

Although it is not clear whether or how the initiative could be implemented, pharmas are taking the threat seriously and have contributed $39 million to a campaign to defeat it. AHF has contributed about $1.3 million to promote the initiative.

AHF also is engaged in a legal battle in Ohio, where Secretary of State Jon Husted has declined to take steps required to place a similar initiative on the ballot. Responding to a complaint filed by attorneys representing PhRMA, Husted has ordered local election officials to recertify petition signatures that are required to place the Ohio Drug Price Relief Act on the ballot.

— STEVE USDIN

More pricing transparency is on the way. The budget bill signed into law in December included instructions for HHS to prepare a more comprehensive report on government spending on prescription drugs.

The report, due in May, will be scrutinized for evidence that Medicare and Medicaid are paying too much for specific drugs or classes of drugs. In any case, it is sure to fuel a new round of headlines and calls for drug price controls.

MESSAGING

BIO, PhRMA and individual companies are using the legislative dead zone created by the presidential campaign to shore up political support in a Congress that includes many members who are unfamiliar with or unsympathetic to the interests of drug developers.

> "IT HAS BEEN CHALLENGING AND CERTAINLY NOT STRAIGHTFORWARD TO IMPLEMENT THOSE KINDS OF MODELS FOR DOCTORS AND HOSPITALS, AND IT WON'T BE EASY FOR DRUGS."
>
> MARK MCCLELLAN, DUKE UNIVERSITY

BIO is also putting the final touches on a media and lobbying campaign emphasizing the value of biopharmaceuticals and the high costs of other healthcare products and services, Ron Cohen, president and CEO of Acorda Therapeutics Inc. and chairman of BIO, told BioCentury.

"There are many, many facts we could point out that would indicate why most of the angst about drug prices is misplaced: where drugs have saved costs overall; that drugs make up 10-14% of overall healthcare costs," Cohen said. "The problem is when you start pointing that out it seems to people you are making excuses for what people believe: drug prices are too high."

Cohen added that this "perception has been deliberately fueled by an active campaign by the health insurance industry to focus attention on drug prices to deflect attention from their own culpability" for designing plans that hit patients with high co-pays and deductibles.

"There has never been a focused effort to deal with these perceptions and misperceptions in a systematic way," Cohen said.

This belief has led BIO to decide to invest in a messaging campaign that will involve advertising in traditional and online media, as well as use of social media, according to Cohen.

"Much of the discussion is one-sided, focusing only on the 10% of healthcare spent on prescription pharmaceuticals, and excluding the other 90%," Kenneth Lisaius, BIO's SVP of communications, told BioCentury. "Our industry will continue to directly respond to those who choose to focus myopically on one small element of what remains a much larger issue. You'll see us increase the volume over the next year."

BIO also plans to create a dialogue with payers and patients, Cohen said.

"We are working on getting a new set of messages out there regarding our commitment to patient access to medicines and the value of what we are producing," he reported. "And we are starting the discussion among stakeholders, now that we hopefully agree to stop pointing fingers, about how to set a value for a drug and set a price that doesn't kill innovation."

Cohen said, "BIO and PhRMA need to be going out in a very deliberate way and changing the way in which we engage with society through media, government, with payer organizations in terms of explaining our story: What is valuable about what we are producing, how are we demonstrating value, and what will we sign up to in terms of demonstrating value going forward."

BIO's challenge, however, may not be to demonstrate the value of its products, but to convince the public, politicians and payers that its prices are fair and sustainable.

Patients and payers understand that curing HCV, and drugs like those that drove President Jimmy Carter's cancer into remission, are valuable. They are concerned by prices that impose what oncologists now call "financial toxicity" on patients, and that make specialty drugs the most rapidly accelerating cost for the healthcare system.

Patient groups, including the National Health Council (NHC), are pushing for federal and state policies that address financial toxicity by preventing insurers from turning deductibles into a wall that prevents many patients from accessing life-sustaining medicines.

Part of this agenda, capping monthly out-of-pocket drug expenses, has made it into Hillary Clinton's campaign platform. Insurance plan design reforms, especially if they are combined with steps to move toward value-based drug pricing, could win bipartisan support if the fall elections usher in a cooler political climate. bc

COMPANIES AND INSTITUTIONS MENTIONED

Acorda Therapeutics Inc. (NASDAQ:ACOR), Ardsley, N.Y.
AIDS Healthcare Foundation (AHF), Los Angeles, Calif.
Biotechnology Innovation Organization (BIO), Washington, D.C.
Duke University, Durham, N.C.
Henry J. Kaiser Family Foundation, Menlo Park, Calif.
Johnson & Johnson (NYSE:JNJ), New Brunswick, N.J.
Merck & Co. Inc. (NYSE:MRK), Kenilworth, N.J.
National Health Council (NHC), Washington, D.C.
National Institutes of Health (NIH), Bethesda, Md.
Novartis AG (NYSE:NVS; SIX:NOVN), Basel, Switzerland
Pharmaceutical Research and Manufacturers of America (PhRMA), Washington, D.C.
Truveris Inc., New York, N.Y.
Turing Pharmaceuticals AG, Zug, Switzerland
U.S. Centers for Medicare and Medicaid Services (CMS), Baltimore, Md.
U.S. Department of Health and Human Services (HHS), Washington, D.C.
U.S. Department of Veterans Affairs (VA), Washington, D.C.
U.S. Food and Drug Administration (FDA), Silver Spring, Md.
Valeant Pharmaceuticals International Inc. (TSX:VRX; NYSE:VRX), Laval, Quebec

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Usdin, S. "Freeing speech." *BioCentury* (2015)

"BECAUSE THERE IS AN APPROVAL PROCESS TO ENSURE BIOEQUIVALENCE AND QUALITY MANUFACTURING, THIS SELF-CORRECTION CAN HAPPEN ONLY AT THE SPEED OF FDA."

GREENE, ANDERSON & SHARFSTEIN, JOHNS HOPKINS

POLITICS, POLICY & LAW

COMPOUNDING PRICES

BY STEVE USDIN, WASHINGTON EDITOR

Joshua Sharfstein, associate dean at the Johns Hopkins Bloomberg School of Public Health, wants to deploy the FDA to battle companies like Turing Pharmaceuticals AG that have enraged the public by obtaining sole U.S. distribution rights to medically important generics and exploiting their monopolies to impose astronomical price increases.

Although some precedent exists for FDA taking steps to facilitate access to lower-cost drugs, the concept is highly contentious within the agency and among public health experts who believe FDA should focus exclusively on the medical and scientific aspects of the products it regulates.

Sharfstein, who served as FDA principal deputy commissioner for the first two years of the Obama administration, outlined his proposals in a commentary co-authored by Bloomberg School colleagues Jeremy Greene and Gerard Anderson that was published this month in *The Journal of the American Medical Association*.

The policy tools Sharfstein and colleagues are proposing — pharmacy compounding and allowing the importation of drugs that haven't been approved by FDA — are at least as controversial as the general principle of FDA intervening to lower prices.

The history of compounding over the past two decades does not inspire confidence. A pattern of safety lapses has been only partially mitigated by legislation passed in 2013 that gives FDA more authority to regulate compounding pharmacies.

The agency has allowed importation of drugs, but because of concerns about the safety of drugs of unknown provenance, it has done so only in extraordinary circumstances to solve urgent medical problems.

THE PROPOSAL

Sharfstein and colleagues suggest that FDA has inadvertently created conditions that allow companies like Turing to pursue a business strategy based on "dominating noncompetitive markets for older drugs and then increasing the price substantially."

They wrote that in a well-functioning market, the strategy would not work because competing products would quickly drive down prices. However, they noted, "because there is an approval process to ensure bioequivalence and quality manufacturing, this self-correction can happen only at the speed of FDA review." FDA has a "massive" backlog of ANDA applications, and it takes years to get a new generic approved, they said.

Sharfstein and colleagues think FDA should formally prioritize review of ANDAs "for essential drugs that can have a major effect on competition and affordability in the market."

The proposal is an extension of the agency's policy of prioritizing reviews of generics to alleviate shortages, Sharfstein told BioCentury.

He assumes that if FDA prioritized its applications, potential competitors would quickly try to exploit the opportunity created by a high-priced generic.

Turing's fiftyfold increase in the price of toxoplasmosis drug Daraprim pyrimethamine brought the strategy of exploiting monopolies on generics to the public's attention. There is no evidence, however, that generics manufacturers have applied or plan to apply to FDA to manufacture pyrimethamine, which has a very small market in the U.S.

The most controversial part of the Bloomberg team's proposal is for FDA to temporarily allow pharmacy compounding and/or importation of off-patent drugs that have been subjected to excessive price hikes while FDA conducts priority reviews of ANDAs from potential competitors. Compounding or importation would be halted after a competing product is approved.

"FDA REVIEW OF MANUFACTURING QUALITY AND BIOEQUIVALENCE DATA IS IMPORTANT. IT IS NOT IN THE INTEREST OF PATIENTS TO CIRCUMVENT THAT PROCESS."

ALLAN COUKELL, PEW CHARITABLE TRUSTS

Sharfstein says compounding can be performed safely under section 503B of the Compounding Quality Act of 2013 that allows pharmacies to register as "outsourcing facilities." Such facilities are subject to more stringent manufacturing quality standards than those governing traditional compounders.

Under the proposal, FDA or some other government entity would identify off-patent drugs that could be monopolized, and then select drugs to include on a list of medicines that could be produced by outsourcing facilities.

Sharfstein also noted that FDA has allowed importation of drugs that haven't been approved in the U.S. to address public health emergencies, including to ameliorate a 2012 shortage of the widely used, potentially life-saving cancer medicine doxorubicin.

FIREWALL

Although the primary purpose of generic and biosimilar drug reviews is to create market conditions that will lower costs, FDA has attempted to maintain a firewall between its regulation of medical products and any consideration of drug pricing.

For example, a November document on FDA's website notes the agency "has no statutory authority to investigate or control" drug prices and suggests that consumers direct any concerns about prices to the Federal Trade Commission.

The firewall has been pierced at least twice during the Obama administration, prompting fierce debates within FDA both times.

In 2009, FDA reviewed an application from URL Pharma Inc. for Colcrys colchicine. Colchicine was first used 3,000 years ago to treat gout, but when URL submitted its marketing application there was no FDA-approved single-ingredient colchicine on the market.

FDA officials knew Colcrys' approval was a double-edged sword. Unapproved colchicine products with inconsistent potency and purity had killed at least 117 Americans, according to FDA, so approval of Colcrys would save lives. It was also certain to result in dramatic price increases that could reduce access.

Some officials argued that the agency lacked authority to consider pricing or access as part of the review, but Sharfstein delayed the approval until URL, now part of Takeda Pharmaceutical Co. Ltd., developed a program to provide access for uninsured patients.

Colcrys was launched at $4.85 per pill, more than 50 times the $0.09 preapproval cost of colchicine. FDA highlighted the company's patient assistance program in communications to patients and physicians, and a year after the approval ordered manufacturers to stop marketing unapproved colchicine products. This was consistent with a policy FDA instituted in 2006 to force the withdrawal of unapproved versions of approved drugs.

While FDA's delay in approving colchicine did not receive much public attention, its involvement in the next drug pricing controversy had a much higher profile.

In February 2011, FDA approved Makena hydroxyprogesterone caproate, a synthetic version of naturally occurring 17 alpha-hydroxyprogesterone (17P), which is prescribed to prevent preterm births.

Makena's sponsor, KV Pharmaceutical Co., set a price of $1,500 per injection for a product that was available from compounding pharmacies for $10-$20 per dose. KV changed its name to Lumara Health Inc., which was acquired by AMAG Pharmaceuticals Inc. in 2014.

Bowing to extraordinary pressure from the White House and Congress to shield Medicaid, Medicare and other payers from the price increase, FDA acted in March 2011 to preserve access to compounded 17P.

Contrary to its 2006 policy on unapproved drugs, FDA said it did not intend to take enforcement action against pharmacies that compounded 17P. It said the decision was intended "to support access to this important drug, at this time and under this unique situation."

CONCERNS

When FDA gave the green light for compounding 17P it was aware of hundreds of serious illnesses and deaths from improperly compounded drugs from 1990 to 2005 and was concerned that the lack of reporting requirements meant that these statistics understated the problem. At the time, however, the risk wasn't widely understood outside the agency.

The dangers of poorly regulated pharmacy compounding became obvious in 2013 when 64 people died and hundreds were sickened by fungal meningitis and other infections caused by contaminated

methylprednisolone produced by the New England Compounding Center.

In response, Congress passed the Compounding Quality Act. The law doesn't give FDA as much authority as the agency felt it needed to ensure the safety of compounded drugs, but it did establish the voluntary 503B "outsourcing" category.

503B outsourcing facilities are subject to higher standards than other compounding pharmacies, but there are no guarantees that the drugs they sell are the same as those produced in FDA-regulated manufacturing facilities.

"As a general matter, we recognize that FDA review of manufacturing quality and bioequivalence data is important. It is not in the interest of patients to circumvent that process," Allan Coukell, senior director for health programs at the Pew Charitable Trusts, told BioCentury.

FDA issued numerous warning letters to registered outsourcing facilities in 2015 for shipping adulterated and misbranded drugs. In some cases facilities have failed to implement promised process improvements, and FDA has forced them to withdraw contaminated products that had been shipped to hospitals and physicians.

Contamination of sterile solutions may only be the most obvious hazard associated with compounded drugs, according to Coukell. "Sterility problems may show up more because of the seriousness of the medical issues and because there is a system to report them to state health departments."

Sub- or superpotency of oral drugs produced in compounding pharmacies would be less likely to be detected, he added. "In some states you don't have to report adverse events associated with a compounded product."

CAMEL'S NOSE

Sharfstein counters criticisms by arguing that FDA should only allow compounding or importation if it was certain that they could be done safely, and that "the benefits outweighed the risks."

The goal, Sharfstein told BioCentury, is to use these tools rarely if ever.

Simply giving FDA the option to battle would-be Turings would serve as a deterrent to price gouging, he said.

But current and former FDA officials told BioCentury they are wary of the proposals both because of the potential risks to patients from compounding and importation, and because of concerns that giving FDA an explicit role in regulating prices would undermine the integrity of its decisions.

Public trust in FDA is predicated on the belief that it bases decisions on medical and scientific criteria, not on economic considerations.

While only a small number of off-patent drugs fit the pyrimethamine and colchicine profiles — medically important, cannot be easily replaced by other generics, and produced by a single company — public outrage over drug prices is not limited to such products.

Creating a process for FDA to help reduce the cost of such drugs puts the camel's nose under the tent, raising the possibility that Congress and the White House would pressure the agency to act to lower the price of new drugs. This raises the possibility that FDA could be perceived as prioritizing economic benefits to society over the medical needs of individual patients. bc

COMPANIES AND INSTITUTIONS MENTIONED

AMAG Pharmaceuticals Inc. (NASDAQ:AMAG), Waltham, Mass.
Federal Trade Commission, Washington, D.C.
Johns Hopkins Bloomberg School of Public Health, Baltimore, Md.
New England Compounding Center, Framingham, Mass.
Pew Charitable Trusts, Washington, D.C.
Takeda Pharmaceutical Co. Ltd. (Tokyo:4502), Osaka, Japan
Turing Pharmaceuticals AG, Zug, Switzerland
U.S. Food and Drug Administration (FDA), Silver Spring, Md.

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