

Modern Healthcare

Civica Rx aims to stabilize fragile pharmaceutical supply chain

By [Alex Kacik](#) | January 19, 2019

Too many times Dr. Martin Makary has had to explain to a patient why he can't prescribe the drug he or she needs.

On a [weekly if not daily](#) basis, doctors like Makary have to navigate around drug shortages caused by a manufacturing hang-up, recall or an unexpected price hike. They must search for alternative therapies, which may not be as effective, trusted or affordable. Clinicians are often in the dark about whether the shortage will be resolved in a day or a month, which makes caring for sick patients that much harder, said Makary, a practicing surgeon and professor of surgery, health policy and management at Johns Hopkins University.

Saline, a sterile version of saltwater used to rehydrate patients, the anesthetic propofol and the anticoagulant heparin—which are used in almost every admission—have consistently been in shortage, he said. This prompts an increasingly frustrating and seemingly unimaginable conversation with patients, Makary said.

“It defies logic that we as a country with all our wealth and power are not able to produce a consistent supply of a common, routine, easy-to-manufacture medication that has been around for a long time,” he said.

CIVICA RX FOUNDING MEMBERS

Announced January 2018

Officially organized in September by Catholic Health Initiatives, the Gary and Mary West Foundation, HCA Healthcare, Intermountain Healthcare, Laura & John Arnold Foundation, Mayo Clinic, the Peterson Center on Healthcare, Providence St. Joseph Health, SSM Health and Trinity Health

Twelve new founding members were added in January, bringing the total to 750 hospitals: Advocate Aurora Health, Allegheny Health Network, Baptist Health South Florida, Franciscan Alliance, Memorial Hermann Health System, NYU Langone Health, Ochsner Health System, Sanford Health, Spectrum Health, St. Luke's University Health Network, Steward Health Care and UnityPoint Health

One potential solution—a provider-owned drug company—has garnered the support of around 750 hospitals and nearly two dozen founding members. Civica Rx is backed by a group of health systems and philanthropic organizations that aim to bring some stability to the pharmaceutical supply chain by producing generic drugs used in nearly every hospital.

One founding member has dropped out—St. Louis-based Ascension—and declined to comment on why, but did confirm its departure.

While Civica Rx has amassed broad support throughout the industry, it faces a series of hurdles as it ramps up. Notably, it must overcome the problems that have vexed generic suppliers stemming from a lack of manufacturing redundancy.

Other stakeholders are making similar moves. Group purchasing and consulting organization Premier, for instance, announced a new company last week called ProvideGx, which has partnered with five generic manufacturers to initially target 60 crucial drugs.

Civica Rx has already sent ripples throughout the industry, said Rob Austin, a director at consulting firm Navigant, whose views echo a hopeful chorus of industry experts who welcome the not-for-profit organization with cautious optimism.

“There are strong barriers to entry,” he said. “But Civica Rx can make a substantial difference in the pricing and supply of generic drugs in three or five years. It may take longer than we would hope but I think it is going to come.”

Daily dose of shortages

Cleveland Clinic pharmacy managers receive a shortage list each day with an average of 25 drugs on it. For about half of those there's a simple substitute of another clinically equivalent generic, while a few require a more creative workaround.

Employees huddle with wholesale distributors and manufacturers to understand the root cause of the shortage. If they find out the organization will be without a critical medication for some time, they try to shuffle supplies throughout their hospital network, update electronic health records accordingly and alert medical staff as they look for alternatives.

THE PERENNIALS

Drugs with persistent shortages:

- Bupivacaine and lidocaine
- Calcium chloride
- Calcium gluconate
- Cefepime
- Epinephrine
- Opiate injectables
- Piperacillin- tazobactam
- Potassium chloride
- Propofol and heparin

Saline
Sodium bicarbonate
Sodium phosphorite

Hospitals and health systems have had to pull injectable drugs like [sodium bicarbonate](#) off crash carts. The sterile form of baking soda is used during advanced cardiac life support and as an antidote to some poisons. The shortage has delayed heart surgeries and compromised other emergency events when a patient's blood is too acidic, which can be fatal without proper treatment.

Cleveland Clinic is always managing anesthetics as well as emergency syringes like epinephrine, sodium phosphorite and lately [opiate injectables](#), although those have gotten better, said Chris Snyder, a Cleveland Clinic pharmacist and drug shortage specialist.

"There have been tremendous issues with lidocaine and bupivacaine," Snyder said. "This is probably the worst we have ever seen in the local anesthetic market."

Civica Rx plans to deliver 14 generic drugs to hospitals and health systems in 2019. It is focused on older sterile injectable drugs, said Martin VanTrieste, CEO of Civica Rx and a former Amgen executive.

The drugs in short supply can vary, though shortages of bupivacaine and lidocaine have persisted since 2011, said Erin Fox, a drug supply expert who's senior director of drug information and support services at University of Utah Health.

Calcium chloride, which is commonly stocked in crash carts for resuscitation, has also been in short supply since 2011. Calcium gluconate, an essential ingredient in IV nutrition for premature babies, seriously ill adults and dialysis patients, has been short since 2012. Cardiac arrhythmia-stopping potassium chloride also has been persistently scarce since 2012.

Shortages of antibiotics used primarily in hospitals for very sick patients like piperacillin-tazobactam have been occurring since 2013 and cefepime since 2014. Sometimes hospitals couldn't get a specific size, and in other cases they couldn't obtain any product, forcing a switch to other antibiotics, Fox said.

These shortages can cost hospitals [valuable resources](#). Finding new suppliers can [lead to errors](#), safety issues or delayed surgeries. Because EHRs require the use of the exact same product in size, formulation and strength, any needed changes due to shortages can require hundreds of hours of updates, she said.

"The key issue is inadequate capacity in manufacturers that are willing to make basic hospital products," Fox said.

Ochsner Health System in New Orleans has seen the frequency of drug shortages significantly increase over the past several years, said Dr. Robert Hart, the system's executive vice president and chief medical officer. "We have resources constantly looking for where the next problem is going to be," he said.

More than 90% of about 1,200 surveyed hospitals reported having to identify alternative therapies to mitigate the impact of drug price increases and shortages, according to a new report from the American Hospital Association, the Federation of American Hospitals and the

American Society of Health-System Pharmacists. A quarter of hospitals had to cut staff to mitigate budget pressures as average drug spending increased by 18.5% between 2015 and 2017. That rate tripled overall medical inflation over that period, resulting in \$1.8 million in new spending for an average hospital. Specifically for drugs in shortage in 2016, average unit prices increased 23.4%.

Fewer manufacturers

Competition has been declining over the past several years because of mergers and acquisitions, said Jeff Rosner, senior director of pharmacy contracting and purchasing at the Cleveland Clinic. More companies are shifting toward higher-profit specialty and orphan drugs, he said.

“They have much smaller markets but the prices they are charging for them are through the roof,” Rosner said, citing drugs like Biogen's spinal muscular atrophy drug Spinraza, which costs \$750,000 for the first year of treatment. “We've lost balance. It's a lot more profitable to make a contracted drug for a branded company as opposed to making generic drugs.”

In addition to capacity problems, there are more predatory actions by opportunistic drugmakers like [Valeant Pharmaceuticals](#), which acquired the rights to the off-patent heart drugs nitroprusside and isoproterenol in 2015 and raised their respective prices 30-fold and 70-fold over three years.

Generic-drug makers have also been accused in a wide-reaching lawsuit of fixing prices.

Even seemingly simple injectables like saline and sodium bicarbonate have proven difficult to produce in large-scale batches that are sterile and particle-free. More than a fifth of abbreviated new drug applications submitted for new generic drugs were denied between 2015 and 2017, according to [FDA data](#) analyzed by [PricewaterhouseCoopers](#). Nearly a third of those applications were denied due to inadequate chemical stability of the drug.

“I think the marketplace lacks strong financial incentives to guard against shortages because when they do occur, prices can go up and revenue can be unchanged,” Makary said.

A shot in the arm

Civica Rx officials promise that some help will come this year.

The older sterile injectables typically do not require bioequivalence studies, meaning they are easier to bring to market.

To get newer generic drugs approved, the FDA requires samples from branded manufacturers, which has been a major impediment for generic-drug developers. Branded-drug makers [haven't given samples](#) of their products to generic manufacturers, throttling the process. That is one tactic the Creates Act aims to eliminate.

For the initial phase, Civica Rx is working with holders of abbreviated new drug applications, or ANDAs, that have the manufacturing capability and capacity to produce the product, VanTrieste

said. Next, the organization plans to acquire or develop its own ANDAs and use contract manufacturers.

Over the longer-term, Civica Rx plans to buy or build its own manufacturing facilities, he said.

Since these aren't new generics, they wouldn't qualify for an expedited abbreviated new drug application process or the 180-day market exclusivity. The FDA is [fast-tracking applications](#) for generic drugs, but only ones that have less than three competitors.

While the endeavor's focus is preventing shortages, bringing more competition could also lower prices. While the first generic competitor typically only prices its product slightly lower than its brand-name counterpart, the price is cut nearly in half when there are two generics on the market, according to the FDA.

The Generic Drug User Fee Amendments [set a goal](#) of approving ANDAs in 10 months, and the FDA has strived to improve communication with manufacturers sooner so they know if there are issues with their application.

“There's not a shortage of ANDAs sitting at the FDA for approval,” said Brian Romig, a director at Navigant, adding that it's an expensive endeavor.

There is also a question of liability when it comes to the manufacturing process. Even though Civica Rx will be subcontracting with an existing generic-drug manufacturer, the organization would still be liable for any quality mishaps. Manufacturing snags and quality concerns have especially been prevalent in the sterile injectable space, evidenced by the roadblocks Pfizer and Baxter Pharmaceuticals have faced that have caused some of the most acute shortages.

Pfizer's McPherson, Kan., plant, where the organization makes a significant portion of the country's [injectable opioids](#) and anesthetics, has been a source of one of the most recent shortages.

The facility, which was acquired as part of the drug manufacturer's acquisition of Hospira, has received multiple [warning letters and citations](#) since 2016. Regulators cited a lack of proper oversight that led to product contamination.

Pfizer has procured additional opioid supply from Sandoz' [Canadian site](#), which has helped bolster supply since August, Pfizer said in a statement. It has restarted production of its pre-filled opioid syringes and is working on releasing product throughout 2019, Pfizer said.

“There tend to be only one or two major manufacturers and if you lose a major market player, which Pfizer tends to be, you really have an issue,” said Cleveland Clinic's Snyder. “Many drugs are made on the same supply line but you don't have true visibility of what is made on the line until after the fact.”

Startup costs

As for the capital required to get Civica Rx going, it should have a minimal impact on the founding members' balance sheets, said Kevin Holloran, a senior director with Fitch Ratings, which has talked with multiple participants.

“I would not expect any negative rating impact whatsoever from being a participant,” he said. “If there were any pressure at all caused by any startup costs, they should be alleviated by the savings on the specific in-need drugs they are targeting.”

Those who buy a particular drug from Civica Rx will have to commit 50% of their annual purchases to the organization at a set price for between five and 10 years.

But Todd Ebert, CEO of the Healthcare Supply Chain Association that represents GPOs, doesn't expect Civica Rx to overshadow GPOs, which will work in tandem with Civica Rx, he said.

“GPO relationships will still be in existence and very strong,” Ebert said. “Civica Rx will have a handful of products for now and hospitals will commit to 50% of that particular product line and use the GPO for the rest. We applaud the fact that they are pursuing a different model. We all want to solve this issue and can learn from each other. Civica Rx could play a much-needed role.”

Other experts agreed. Prices will likely fluctuate once the coalition gets up and running, they said.

“Managing drug shortages is so costly from a labor and informatics perspective that hospitals would likely be willing to pay more for a reliable supply,” Fox said.

Critics are skeptical that hospitals and health systems will be willing to make a long-term commitment, particularly if a cheaper product comes out. There will still be too few manufacturers.

The manufacturer that Civica Rx contracts with would also be susceptible to natural disasters or contaminated raw products, which are largely sourced from [China and India](#) where oversight isn't as strong. Then providers would have a commitment to a supplier that can't supply, skeptics said.

But many are invested in seeing Civica Rx succeed.

“It would require some significant momentum in order to disrupt the marketplace, but if it does, it would be healthy,” Makary said.

Alex Kacik

Alex Kacik is the hospital operations reporter for Modern Healthcare in Chicago. Aside from hospital operations, he covers supply chain, legal and finance. Before joining Modern Healthcare in 2017, Kacik covered various business beats for seven years in the Santa Barbara, California region. He received a bachelor's degree in journalism from Cal Poly San Luis Obispo in Central California.