

Sometimes, Drugs Are Not Costly Enough

By AUSTIN FRAKT

For some of the most important drugs, prices may be too low.

You hear a lot about high drug prices. You hear politicians calling for lower drug prices. But you may not be hearing about how low prices contribute to drug shortages.

The drugs most prone to shortage are generic injectable ones, administered to patients in the hospital or a doctor's office. They include anticancer agents, heart attack medications and anesthetics, many used in life-threatening, emergency situations. When such drugs are in short supply, they cause dangerous delays in care as hospitals seek alternatives. Even when good substitutes can be found — and sometimes they cannot — they may be less familiar to doctors, come with different side effects or not work as well, all of which pose risk to patients.

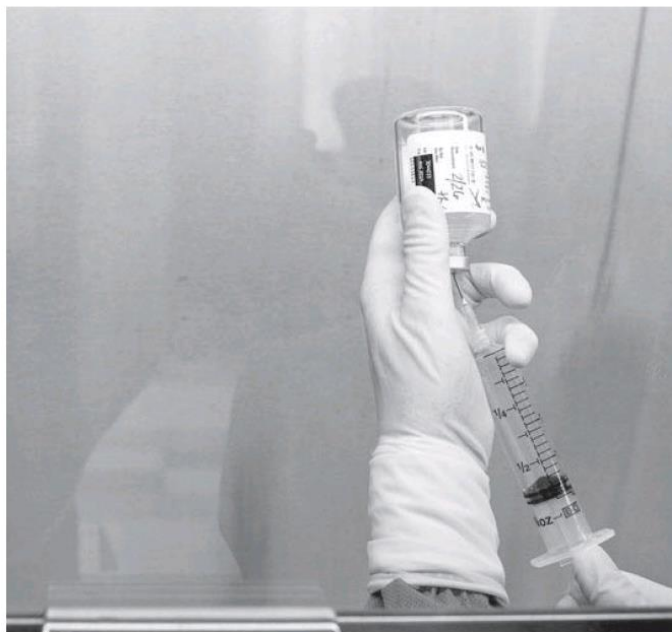
For example, when morphine is in short supply, doctors might switch to hydromorphone, an alternative opiate painkiller. Hydromorphone is seven times more powerful than morphine. Failing to account for that difference can

Delays can be dangerous when supplies run short.

kill. In 2011, during a morphine shortage, two fatalities were linked to the accidental dosing of hydromorphone as if it were morphine. This year, the generic injectable form of nitroglycerin — used to treat serious heart attacks in emergency departments — is among the drugs in shortage, prompting the Food and Drug Administration to seek additional supplies overseas.

Hospital pharmacists say drug shortages are their biggest problem. “Clinicians are spending time

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MATT ROTH FOR THE NEW YORK TIMES

The problem of shortages is most serious with generic injectable drugs, which are costly to manufacture.

making sure patients aren't impacted by drug shortages,” said Erin Fox, a pharmacist and director of the University of Utah's Drug Information Service, which tracks drug shortages. “But it's incredibly frustrating to not have access to basic essentials.”

The number of drugs in short supply peaked in 2014 at 320, the vast majority of which were generic injectables. That doesn't mean the problem has faded. According to a recent study in the journal *Health Affairs* by Ms. Fox and colleagues, the number of emergency and critical care drugs in short supply has grown in recent years. These include pain medications, sedatives, electrolyte solutions, antibiotics, antidotes and drugs that undo the effects of anesthesia.

According to another recent study by Ms. Fox and colleagues, one-third of drugs in short supply are used in emergency departments to treat critical health problems like respiratory distress, heart problems and overdoses. Half of drugs used by emergency physicians that are in short supply are for life-threatening conditions, and 10 percent have no good

substitutes. Such supply disruptions are not brief — most last at least nine months, according to the study — so they affect many patients.

Generic injectables are prone to shortage because of low profit margins and high production costs. Except in unusual circumstances, generic drugs — whether injectable or oral — have low profit margins because no manufacturer retains exclusive rights to produce them. Were prices and profit margins to rise high enough to justify the upfront investment of drug production, other manufacturers would enter the market. The additional competition would then push prices and profit margins back down again.

Prices are also held in check by group purchasing organizations. They consolidate drug orders across hospitals, directing large volumes to a small number of manufacturers that provide the best deals. This also concentrates the market in a few manufacturers. Most generic injectables are produced by three or fewer companies. When a manufacturing problem arises at one of them, it threatens a large pro-

portion of supply, and sometimes for dozens of drugs at a time.

Facing low prices, these few manufacturers must keep tight control over capacity in order to turn a small profit. They cannot afford to produce more drugs than will sell, nor can they afford for backup plants and production lines to sit idle waiting to fill a shortage. Instead, manufacturers use whatever capacity and resources they have to produce more profitable products. When a manufacturing problem arises that forces a halt in production, there is no backup, causing a shortage.

Generic injectables cost more to make than generic oral drugs. They must be more sterile than oral drugs because they are injected directly into the blood, spine or eye. They do not pass through the digestive system, which confers a degree of protection. Getting injectable production started and approved by regulators can take years and can cost hundreds of millions of dollars. Even if prices and profit margins rise during a shortage, they typically don't rise high enough or for long enough to coax manufacturers into adding capacity. This is why some drugs are persistently in short supply. Fewer shortages arise in Europe, where generic injectable prices are higher.

A 2012 law gave the F.D.A. new tools and responsibilities to fight shortages. Since then, the number of new shortages that arise has come down and some older ones have been resolved. The F.D.A. averted 80 percent of new, potential shortages in 2013, for example. It did so by accelerating approvals for alternative drugs, advising manufacturers on how to overcome shortages and devising workarounds to purify drugs contaminated during faulty production.

Even with this progress, shortages still arise — nearly 200 of them last year. The one thing the F.D.A. does not have the authority to do is raise drug prices. For most drugs, we wouldn't want them to. For some critical, generic injectables, maybe it's an idea worth considering.