

Drug Shortages Spark Use of Compounders

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WASHINGTON – As drug shortages continue to plague the specialty of anesthesiology, compounding pharmacies – such as the one [implicated in the ongoing meningitis outbreak](#) – may be playing a key supply role, clinicians said here.

Although some measures taken by the federal government and advocacy groups have assuaged shortages, clinicians at the American Society of Anesthesiologists (ASA) meeting here said they're still feeling the pinch and have been searching for alternatives.



"Compounding pharmacies have fit a niche in terms of getting medications to patients," John Dombrowski, MD, chair of communications for ASA and director of the Washington Pain Clinic, told *MedPage Today*.

Steven Gayer, MD, professor of anesthesiology at the University of Miami, agreed that in times of shortage, "the correct answer is to find a compounding pharmacy."

Although compounders are focused on providing tailored drugs for specific patient needs, David Ball, a spokesperson for the International Academy of Compounding Pharmacists, confirmed that these pharmacies have been picking up some of the slack during shortages.

"Compounders have regularly been called on to make those medications that are commercially unavailable," Ball said. They have access to raw materials, and with orders from patients -- or from hospitals for specific patients -- they can help disseminate drugs when they're needed most.

Some of these pharmacies have even adopted a direct-to-consumer approach. The Professional Compounding Centers of America, which supplies compounders with raw materials, has a [section on its website](#) that instructs patients how to find their local compounders if their medications are out of stock.

But these companies have [come under fire recently](#) for their role in the meningitis outbreak, which has [sickened 247 people](#) and killed 19 people in 15 states. The affected patients were given contaminated spinal injections of methylprednisolone acetate from the New England Compounding Center in Framingham, Mass., which was [raided by federal investigators](#) on Tuesday.

Methylprednisolone shots are indeed in short supply, according to the American Society of Health-System Pharmacists' drug shortage tracker. Manufacturers Sandoz and Teva have all shipments on back order with vague information as to when they'll be available again -- putting pressure on pain specialists to find other sources.

At the ASA meeting, clinicians were urged to check out those compounding pharmacies before making any purchases. Gayer said the U.S. Pharmacopeia has specific guidelines on compounding, with U.S.P. 797 -- a guidance focused on sterile preparation -- being especially relevant.

These entities are supposed to be regulated by individual states, with very little oversight from the FDA. But some experts have questioned whether compounders [need greater oversight](#), especially as the line that separates a compounder and a larger producer blurs.

Gray Market

The shortage has also raised the specter of a "gray market" for drugs, in which smaller distributors may be marking up the prices on drugs in short supply.

Capt. Valerie Jensen, RPh, associate director of the Drug Shortage Program at the FDA's Center for Drug Evaluation and Research, said during a panel at the ASA meeting that it's "not clear what, if any, laws are being broken" in that process, and added that her agency is sending all gray-market reports to the Department of Justice.

Some clinicians believe, however, that the prices aren't marked up; they just reflect normal profit margins when product isn't bought in bulk, as with larger distributors.

Maximizing Supply

Anesthesiologists are no strangers to making optimal use of supplies. Many injectable drugs used in the operating room come in single-use vials, though these often contain larger amounts of product than needed for a single patient.

For instance, propofol (Diprivan) – which faced shortages last year and is still used conservatively in operating rooms – often comes in 100-cc or 50-cc vials, when the average patient typically needs only 20 cc's.

'Repackaging' doses in the operating room has been shown to increase the risk of infection in the past, but some clinicians may feel pressured to split up the larger vials in times of shortage to maximize the number of patients who have access to care, Joel Zivot, MD, medical director of the cardiothoracic intensive care unit at Emory University in Atlanta, told *MedPage Today*.

Many anesthesiologists have called for smaller packaging, though that's been a challenge given it increases production costs on generic agents that are less profitable to begin with.

Causes Still Unclear

Officials from the FDA continue to point to the same constellation of contributors to the drug shortage problem -- problems at generic manufacturing plants, a lack of financial incentives to make generics, and too few manufacturers to cover demand as more drugs come off patent.

Zivot said that drug pricing contracts between group purchasing organizations (GPOs) and manufacturers may have a hand in diminishing incentives for making generic drugs.

Representing multiple hospitals, GPOs have the leverage to negotiate prices that smaller organizations wouldn't have on their own. As prices fall, manufacturers have less incentive to produce those drugs, he said.

"Fundamentally, this is a broken market," Zivot said. "There are not enough buyers and not enough sellers," he said, noting that three major GPOs cover the bulk of U.S. hospitals and fewer companies are producing generics.

Some Progress

The FDA's Jensen said the agency's staff of 11 employees dedicated solely to drug shortages has taken several steps to mitigate the crisis, most notably a mandatory notification requirement that demands manufacturers tell the FDA at least 6 months before they plan on taking any specific product offline, if they are the only company producing that product.

They also have to report to FDA all disruptions in production within 6 months, Jensen said, though the agency is currently swimming in hundreds of reports per month -- even for just minor issues, she said.

The agency has also facilitated emergency imports of certain drugs, as was the case with propofol coming in from Europe, though the agency "knows it's not where it should be" with the levels of propofol available in the U.S.

And since many anesthesiology drugs are controlled substances, Jensen said FDA has been working with the Drug Enforcement Administration to make exceptions with drug quotas so capable manufacturers can make extra supplies.

She said the agency prevented 38 drug shortages in 2010 and even more -- 195 -- in 2011. But anesthesiologists such as Jeff Jacobs, MD, of the Cleveland Clinic Florida, say their practice is still hampered: "I don't think we're at all out of the woods with the drug shortage situation."

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