THE PHARMACEUTICAL CONUNDRUM

Your patients ask you why their medications are so expensive or why they are having a difficult time obtaining them. Physicians ask why are the costs of my patient's medications escalating so rapidly, why are drugs that used to be relatively inexpensive now prohibitive, and why are there so many drug shortages? The answer is complex and often shrouded in mystery and nuance. A congressional report released on March 26, 2018 found that the prices of the top 20 most commonly prescribed drugs for seniors had risen at nearly 10 times the rate of inflation over the past five years.

Drug shortages are perhaps the easiest to identify and understand. Shortages stem from supply disruptions or constrained manufacturing capacity. Supply disruptions result from raw material or component shortages, quality glitches, change or loss of a manufacturing site, rapid increase in demand or popularity, product discontinuance for economic or strategic positioning relative to other product lines, natural disasters, aging plants especially when combined with high regulatory FDA standards, hoarding as supplies narrow, and approval delays. Several factors may be in play at the same time; the hurricane impact on Puerto Rico devastated power grids and transport that prevented a key plant from manufacturing the rubber access part of saline bags. Obviously, no shortage of saline, water, or plastic in general, but the multifactorial simultaneous impact prevented one of few suppliers from providing a basic medical product. Voluntary recall of select lots of propofol manufactured by Hospira was issued as a result of possible contamination with particulate matter, and the shortage lasted several months.

Constrained manufacturing capacity occurs with limited manufacturing for a product, increase in the number of generic drugs, facility demand for a large number of relatively low-volume drugs that require more frequent changeovers, subsequent changeover delays between service lines, just-in-time inventory stocking strategies by facilities that do not sync with manufacturing production schedules, and liability concerns. Currently, only three pharmaceutical companies account for 70% of the sterile injectable products manufactured in the United States, so the queues are complex.

I need not explain liability exposure to this audience, but I will share one example. The manufacturers' marketing of oversized vials may have contributed to a hepatitis C outbreak linked to contaminated drugs due to the practice of reusing such vials, which inherently poses a risk of infectious contamination. Over the packaging and marketing issue, two partnering companies paid $356 million and $144 million to a single patient! The precedent had a chilling effect on companies making drugs with a high liability risk, especially when the court system unfairly holds pharmaceutical manufacturers responsible for the misuse of their products.

Now for the more difficult part of identifying root causes of cost escalation: old drugs that have been purchased by both venture capitalists and mainstream companies; some widely distributed, and some have limited markets qualifying as orphan drugs, which were granted special status since they treat rare diseases affecting fewer than 200,000 patients. An example of a widely used medicine with a price increase shocker is the 5,000% price increase of AIDS-related treatment

called Daraprim when acquired by a tiny firm run by a former hedge fund manager named Martin Shkreli. Even mainstream companies are looking to exploit orphan drugs : the 1952 drug Acthar, used primarily to treat infantile spasms, was purchased by Mallinckrodt from Questcor for $5.6B and is now promoted to treat multiple sclerosis and other conditions; 3,100 Part D users went from 17.5 to 23.7 uses per year at $38,000 in 2015 after costing $1,650 in 2007, and the Medicare spending on Acthar went from ~$50M to over $500M between 2011 and 2015.

Common generic mediations have also rapidly escalated in cost. Some I have commonly used in the OR include furosemide, succinylcholine, verapamil, and neostigmine; they have increased from 209 to 3,946%. Brand names have also rapidly increased. Some are common chronically used lifesaving drugs such as Insulin; the yearly treatment cost of Humulin-R increased from an average of $2,487 at the end of 2005 to $15,860 by the end of 2015. None of these increases have been linked with incremental production or regulatory costs; the increases are more related to distribution chain relationships. The old supply chain was built on many suppliers dealing with many distributors selling directly to many providers while the new chain is built on a highly concentrated sector. With corporate mergers and consolidations, 70% of the injectable drug market is now controlled by just three companies. While the trade group Pharmaceutical Research and Manufacturers Association (PhRMA) members include mainstream manufacturers, some of the smaller companies in the news are not members (e.g., Mylan of EpiPen). Furthermore, the pharmaceutical distributors are dominated by just four group purchasing organizations or GPOs (Vizient, Premier, Healthtrust, and Intalere), and they have been joined by a new middleman in the form of pharmacy benefit managers or PBMs (CVS Health, Express Scripts, and Optum RX).

Distribution chain relationships suffer from a lack of transparency. Things that would be patently illegal in some industries are protected by the Group Purchasing Organization (GPO/PBM) Kickback Safe Harbor law under US Code 42 CFR § 1001.952. The law permits payment of market fees to position one company to “be on the list” exclusively. Hospitals can benefit from special marketing incentives and packages with preferred corporate Board seats, rebates, pre-bates, sharebacks, and compliance fees. Some of these hospital-pharmaceutical relationships are coming under closer government scrutiny. Finally, some PBM contracts prevent the pharmacist from informing patients that their medication may be less expensive if they do not use their insurance (e.g., prescription copay is more than the cash price) in practices that are known as “clawbacks” and “gag clauses.”

So how do the shortages and the distribution chain interlink? An example is fentanyl, which is commonly, and legally, used in the OR and is certainly not an orphan or limited use medication. Pfizer acquired the fentanyl rights from Hospira, and then halted production at a Kansas facility. Pfizer thus ended up with a 60% fentanyl market share, which is in the top two out of 10 important anesthetics.

At our AMA, resolutions will be offered at the HOD, and our CMS is engaged on the pharmaceutical cost issue with past reports (CMS 7-A-18, CMS 2-A-18) and more to come Also, the TruthinRx campaign advocates for greater transparency in prescription drug pricing. The

Physicians Against Drug Shortage website has links to a number of articles if you want to take a deeper dive; they are actively involved in trying to repeal the safe harbor laws. The AMA Board of Trustees decided not to act upon a MSS resolution asking for repeal of these laws.

In Congress, there is bipartisan sponsorship of bills to make "gag" clauses illegal. So, stay tuned and get your patients involved in the emerging action models since both patients and physicians are victims of the drug pricing conundrum.

Your thoughts and suggestions?

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