STATEMENT

OF

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BEFORE THE

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INTRODUCTION

Mr. Chairman and Members of the Committee, I am Dr. Sherry Glied, Assistant Secretary for Planning and Evaluation at the U.S. Department of Health and Human Services. I am honored to be here today to discuss the economics of drug shortages.

For some patients, a change in treatment regimen because an important medication is not available can seriously reduce the quality of care they receive and threaten their ability to get better. We have heard the stories of a number of people who have faced this problem. Patients, like Jay Cuetara, a cancer patient from California with whom I met earlier this fall, are the ones who suffer when the center where they receive chemotherapy runs out of the drugs used to treat their cancer.

The Food and Drug Administration (FDA) has successfully prevented 233 drug shortages since the beginning of 2010 and is taking additional actions to address drug shortages in response to the President's October 31 Executive Order. In the four weeks following the issuance of the Executive Order, FDA has received 61 notifications, a six-fold increase over the average notifications per month in the previous 10 months.

Drug shortages have been increasing in frequency and severity in recent years and are adversely affecting patient care. A small number of drugs in the U.S. experience a shortage in any given year, but the number of reported prescription drug shortages in the United States has nearly tripled between 2005 and 2010, increasing from 61 to 178. In 2011, FDA has continued to see an increasing number of shortages, particularly among older sterile injectable drugs, including cancer drugs, anesthetics for surgery, drugs for emergency medicine, and electrolytes for intravenous feeding. There are many causes to this challenging problem and addressing this significant public health threat requires the urgent attention of industry, other stakeholders, and government.

BACKGROUND

Market Behavior

Firms have been increasing their levels of manufacturing capacity utilization to accommodate the increase in the volume of chemotherapy drugs administered and the expansion of products available for generic manufacturing because of patent expiration. Shortages have been concentrated in drugs where the volume of sales was declining in the years preceding the shortage, suggesting that manufacturers are diverting capacity from shrinking lines of business to growing ones. Quality problems, potentially caused by the high level of capacity utilization, have led some plants to shut down. A recent report by FDA found that quality problems at drug manufacturing facilities resulting in disruptions in supply were the leading cause of drug shortages, accounting for 43% of all shortages. Firms have not responded quickly to changes in demand and prices in the sterile injectable drug industry by building new plant capacity because of the high fixed costs of specialized production. Furthermore, because shortages are generally uncommon and occur in drugs for which capacity is highly specialized, and because there are few penalties for failing to supply contracted drugs, there is no financial return to manufacturers

from investing in excess capacity – that is, capacity that is not used outside a supply shortage, and thus earns no revenue except during a supply shortage.

Generic drug manufacturers must make strategic decisions about how to deploy existing production capacity among products, based on their expectations about what choices their competitors will make and what demand will be. In general, manufacturers will prefer to concentrate on markets with fewer competitors, where they are likely to face less price competition. Conversely, purchasers, such as GPOs, will prefer that multiple competitors produce each product. If manufacturers misjudge their competitors' choices, there may be excess supply and depressed prices for some drugs and insufficient supply and shortages of others. In small markets, such as those for sterile injectable drugs, these decisions can lead to considerable volatility in the market.

Why do Shortages occur in the Prescription Drug Market?

The prescription drug and vaccine market is characterized by sporadic shortages of individual drugs and occasional periods during which many drugs in a class are in shortage. Although product shortages usually lead prices to rise, consumers to buy less, and producers to manufacture more, that process does not happen in the markets for some medically necessary drugs, especially sterile injectable drugs. By and large, neither the supply nor the demand for medically necessary drugs responds quickly when the prices of these drugs rise.

By definition, these drugs are medically necessary, so they have few substitutes and patients cannot generally shift their use over time. Unlike consumers of other goods and services, patients, hospitals, and physicians generally do not change treatment patterns when prices rise.

Suppliers are also quite insensitive to changes in price, particularly in the short-run. The kinds of medicines that are in shortage are produced using costly, specialized equipment and require complex production processes that must meet Current Good Manufacturing Practice guidelines. Manufacturers can and usually do substitute products within a class using the same production line, but in most cases, each individual drug requires regulatory approvals, including manufacturing controls, which are limited to that particular drug. It generally takes a long time – years in some cases – for the industry to increase capacity in response to an increase in prices. If the increase in prices is expected to be temporary (as would be expected in the case of a shortage due to a production line disruption), investments in increased capacity are unlikely to occur. In the longer run – over a period of 2-3 years, for example – supply will be much more responsive to price.

This low level of price responsiveness on both the demand and supply sides of the market for many medically-necessary products means that any changes from historical patterns in supply or demand can lead to shortages of these drugs.

The Case of Sterile Injectable Cancer Drugs: Supply and Demand

In most cases, sterile injectable drugs are not purchased directly by patients or reimbursed directly by insurance. Rather, these drugs are purchased by health care providers (generally hospitals and physicians). Providers are paid for the delivery of the service that includes the drug. Public and private insurers also pay a separate fee to compensate for the cost of the drug.

Under the Medicare program, the separate fees for sterile injectable drugs generally are paid under Part B.

Most hospitals and physicians do not purchase sterile injectable drugs directly from the manufacturer. Rather, these drugs are purchased through group purchasing organizations (GPOs), which negotiate prices with manufacturers on behalf of their clients. GPOs do not take physical possession of the drugs. Instead, a wholesaler takes possession of the drug and then sells the drugs to hospitals and physicians at the GPO negotiated price.

While GPOs negotiate the lowest prices they can with manufacturers, based on anticipated volume of sales, their clients are not compelled to purchase drugs from a contracted manufacturer, so the GPO contracts do not necessarily contain minimum quantity guarantees. GPO contracts are generally in place for years and typically include price adjustment clauses. If a GPO is offered a lower price by a competing manufacturer, the original contracted manufacturer has a right of first refusal to match the new price. GPO contracts also typically include failure-to-supply clauses. These clauses generally require the manufacturer to reimburse the GPO for the difference between the negotiated price and the purchased price when providers must buy the drug from another source. These failure-to-supply clauses, however, provide no reimbursement if there are no alternative sources for the drug, do not reimburse for resources expended looking for other sources, and are of limited duration.

Manufacture of generic sterile injectable drugs is a concentrated market with 7 manufacturers making up a large percentage of the market. Most of the production of a given drug is by three or fewer manufacturers. Analysis of a sample of 33 generic sterile injectable cancer drugs shows that for 28 of these drugs, at least 90 percent of unit sales in 2010 were made by 3 or fewer manufacturers.[1] These manufacturers typically each operate a small number of facilities at which injectable drugs can be produced. These facilities, in turn, each contain several manufacturing lines. A particular drug can be produced on one or more of these lines in runs that may last from hours to weeks. The same line may be used for multiple different drugs produced in separate batches; however, certain drugs (including cytotoxic drugs) may only be produced on certain types of lines and in certain types of facilities, so the extent of substitution is limited.

It is important to note that the low price responsiveness of demand for sterile injectable drugs also has implications for inventories and capacity decisions. If there is an excess supply of a particular drug, there may be no market for it, even at a low price. The combination of limited ability to compel supply (through failure-to-supply clauses or contractual breach provisions) and low price responsiveness means that manufacturers face an asymmetry of incentives: there is little cost (except reputational) of producing too little of one drug (rather than another), but a potentially high cost of producing too much of that drug.

[1] National Cancer Institute analysis of IMS National Sales Perspectives. In *Economic Analysis of the Causes of Drug Shortages,* U.S. Department of Health and Human Services, Office of the Assistant Secretary for Planning and Evaluation, October 2011, footnote 10.

ASPE recently released a report on drug shortages that focused on sterile injectable cancer drugs, one of the classes of drugs where there are many shortages.[2] The market for sterile injectable cancer drugs is robust and growing. FDA analysis of IMS data shows that the number of vials of sterile injectable cancer drugs shipped between 2006 and 2010 increased by 14%, in part because of the aging of the population. Similarly, ASPE analysis of Medicare Part B data shows that between 2006 and 2011, the volume of services for sterile injectable cancer drugs increased by about 20%.

That increase in volume, however, did not occur across all sterile injectable cancer drugs. Using Part B data, ASPE compared the volume of services prior to shortages for sterile injectable cancer drugs that did and did not experience a shortage. On average, drugs that subsequently experienced a shortage are those in which the volume of sales was declining in the 2006-2008 period prior to the shortages. Drugs that have not experienced a shortage since 2008 had an average 11% increase in volumes of services over this period, and a similar increase in the 2008-2011 period that followed. The results suggest that manufacturers with limited capacity may be making strategic decisions about which drugs to produce when faced with falling demand for particular drugs.

The Case of Sterile Injectable Cancer Drugs: Changes in Market Structure and Production Capacity

Manufacturers can increase their portfolio of generic sterile injectable drugs by filing an abbreviated new drug application (ANDA) with the FDA, which must be approved before the manufacturer can market the generic drug. More ANDA approvals mean that manufacturers have more drugs to choose to manufacture with their existing capacity and therefore, manufacturers may substitute newer drugs for other drugs. Alternatively, they may increase the rate at which they make use of their existing manufacturing capacity. There was a substantial increase in the number of new injectable ANDA approvals beginning in 2008 (prior to the increase in sterile injectable drug shortages).

While the overall market for sterile injectable cancer drugs increased by 14% between 2006 and 2010, the number of vials sold by generic drug manufacturers increased much more rapidly – by nearly 30%. Over this period, the overall generic sterile injectable drug market (including cancer drugs and other classes of products) expanded by 52%. Some of this expansion was accompanied by reductions in brand manufacturers' production of these drugs.

Our analysis showed that generic manufacturers have expanded not only the volume of product they produce but also the range. In every year between 2006 and 2010, the number of new combinations in the market (a manufacturer producing a drug that it had not previously produced) exceeded the number of exits.

Expansion of the scope of production is also evident in the decisions of leading manufacturers to increase future manufacturing capacity. Several leading manufacturers of generic sterile injectable drugs indicated that they are upgrading existing facilities or building new facilities to

[2] U.S. Department of Health and Human Services, Office of the Assistant Secretary for Planning and Evaluation, *Economic Analysis of the Causes of Drug Shortages*, October 2011. http://aspe.hhs.gov/sp/reports/2011/drugshortages/ib.shtml

serve this market. According to news reports and discussions with manufacturers, Hospira is investing $65 million in capital improvements in sterile injectable drug manufacturing sites, Teva is opening a new manufacturing site, and Ben Venue is opening a new, expanded facility to replace an older manufacturing facility.[3] These investments will increase capacity in both older and newer generic sterile injectable drugs.

Unfortunately, this new capacity is unlikely to come online for at least another 18 months. Meanwhile, when there is little excess manufacturing capacity, producing a new drug will often require manufacturers to reduce or stop production of another drug or to operate at a much higher than normal level of capacity utilization.

Increasing utilization of capacity is a good way of expanding supply in the short-run, but poses risks. High rates of capacity utilization may also limit the ability of manufacturers to perform routine maintenance and keep facilities in good order.[4] A recent report by FDA found that quality problems at drug manufacturing facilities resulting in disruptions in supply were the leading cause of drug shortages, accounting for 43% of all shortages.[5]

Supply Disruptions

The structure of the sterile injectable market, the recent expansion in volume and scope, and the consequent very high level of capacity utilization, mean that small disruptions to supply – such as may occur because of quality problems – which would otherwise be absorbed through diversion of capacity, can lead to cascading and persistent shortages.

Over time, entry and expansions in capacity in the industry, should lead to a situation where shortages due to supply disruptions are sporadic and rare. In the current environment, where capacity is severely constrained, shortages induced by disruptions can cascade throughout the sector and persist for long periods of time.

RECOMMENDATIONS

The administration is doing everything in its power to address the shortages administratively. There a few areas where additional authority or action by Congress may be needed or where the private sector can take steps. Based on our examination of the underlying factors that lead to periods of shortage in the prescription drug market, and particularly the underlying market factors that have contributed to the current shortages in the area of sterile injectable drugs, we offer a few recommendations.

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[3] News reports and personal communication with manufacturers. In *Economic Analysis of the Causes of Drug Shortages,* U.S. Department of Health and Human Services, Office of the Assistant Secretary for Planning and Evaluation, October 2011, footnotes 16-17.

[4] Donald Gross, John F. Shortle, James M. Thompson, and Carl M. Harris, *Fundamentals of Queuing Theory*, Fourth Edition, John Wiley & Sons, Inc., Hoboken, N.J., 2008.

[5] U.S. Food and Drug Administration, *A Review of FDA's Approach to Medical Product Shortages,* October 2011. http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/ucm275051.htm

Policymakers must balance the short-run benefits of tailoring regulatory responses to specific situations against the risk of strategic behavior and consequent reductions in competition in the long run.

Steps that both expedite expansion of supply and maintain product quality in sectors with high capacity utilization could reduce the risk of shortages not only in the current situation, but in the future as well. To facilitate this, FDA can expedite review of new manufacturing capacity in this area, and we understand that FDA is already doing this and committed to continuing to do so.

Private organizations that purchase drugs (including GPOs), can help to alleviate future shortages by negotiating with drug manufacturers to strengthen the failure-to-supply requirements in their contracts. Such contractual changes are likely to incentivize drug manufacturers to invest in extra capacity of both production lines and active pharmaceutical ingredients.

As part of the Administration's broader effort to work with manufacturers, health care providers, and other stakeholders to prevent drug shortages, the President has directed the FDA to take steps that will help to prevent and reduce current and future disruptions in the supply of lifesaving medicines and FDA is responding to this directive.

The Administration also announced on October 31, 2011, its support for bipartisan legislation (S. 296 and H.R. 2245) that would require all prescription drug shortages to be reported to FDA and would give FDA new authority to enforce these requirements.

SUMMARY

In summary, the current class-wide shortages in the sterile injectable drug industry appear to be a consequence of a substantial expansion in the scope and volume of products produced by the industry that has occurred over a short period of time, without a corresponding expansion in manufacturing capacity. The current shortages will likely be resolved when new supply sources come online as the manufacturing industry increases its capacity. In the meantime, the FDA's Drug Shortage Program is working diligently with manufacturers and other stakeholders to mitigate the effects of the shortages and the Administration is doing everything in its power to address shortages administratively.

I appreciate the opportunity to speak with you about our analysis of drug shortages. I would be happy to respond to any questions.