AN ECONOMIC ASSESSMENT OF THE CAUSES AND POLICY IMPLICATIONS OF CURRENT SPECIALTY DRUG SHORTAGES

Rena M. Conti, Ph.D.
Assistant Professor of Health Policy and Economics
The University of Chicago

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Chairman Baucus, Senator Hatch and members of Senate Finance Committee, it is my honor to speak to you today about the causes of drug shortages and potential policy responses. I am an assistant professor of health policy and economics at the University of Chicago. I teach graduate level courses on the economics and regulation of the pharmaceutical industry and health economics. My research work examines the financing and organization of medical care, with an emphasis on the use of specialty drugs. My remarks will focus on the supply of and demand for physician administered generic specialty drugs. Some of my remarks are specific to the oncology drug market.

SUMMARY

The use of drugs to treat disease is central to contemporary medical practice. Most drugs in short supply in the United States (US) are physician-administered cancer drugs and lost patent protection prior to 2000. Many of these drugs also have alternative therapeutic substitutes. The presence of shortages appears to be sustained over a long period of time and there is variation in the presence of drugs shortage by physician practice type and by geography. These features suggest that aspects of the supply of, or the demand for, these therapies may constrain competitive market behavior. Empirical research on the organization and financing of the generic supply of specialty drugs and the determinants of demand for these drugs by domestic and international markets is in its infancy. My assessment of the causes of current shortages suggests the highly competitive global market for the supply of generic specialty drugs, and firms' limited excess capacity to produce these drugs and absorb sudden alterations in the cost of production, are largely to blame. Furthermore, the unique nature of purchasing specialty drugs restricts the ability of some providers to access the limited supply of these drugs at reasonable prices. Contemporary oncology practice is characterized by a strong professional drive to adhere to current practice guidelines. Medicare's reimbursement practices act to favor the use of newer, higher cost cancer drugs. Numerous remedies have been proposed to ameliorate specialty drug shortages. They include: increasing reimbursement to oncologists in the US to increase demand for drugs in short supply, eliminating purchasing channels that force significant price concessions from manufacturers and aggravate geographic variations in drug shortage, and levying penalties on generic manufacturers to ensure the supply of selected medically necessary drugs. My evaluation of these proposed policies suggest each proposal entails significant uncertainty regarding the intended and unintended consequences of their adoption. The adoption of any one of these proposals would likely not substantially impact the availability of current drugs in short supply for all physicians or alleviate the market conditions that may produce generic specialty drug shortages in the future.

INTRODUCTION

The use of drugs to treat disease is central to contemporary specialty medical practice. The majority of drugs in short supply in the US are cancer drugs. Oncology drug shortages are of critical national policy concern since cancer is the second leading cause of death in the US. Fortunately, only a limited number of drug shortages have caused serious safety concerns related to both their availability and the mis-dosing of alternatives. The presence of shortages appears to be sustained over a long period of time and there is variation in the presence of drug shortages by physician practice type and by geography. Most specialty drugs in short supply lost patent protection prior to 2000 and consequently, face generic competition. The patent expiration and consequent entry of generic versions of high priced drugs is considered to be an important cost-containment policy in the US.

These features of current specialty drug shortages suggest there are aspects of the supply of or the demand for these therapies that constrain competitive market behavior. In economic terms, a shortage exists when, at any given market price, quantity demanded by purchasers exceeds the quantity supplied by manufacturers. In a competitive private industry, profit-maximizing firms would raise price, consumers would be willing to pay this increased price for a medically necessary therapy, and over time suppliers would increase the quantity supplied, eventually eliminating shortages. In this testimony, I review these unique aspects of the financing and organization of infused specialty drug markets. I then discuss he proposed tools at the disposal of Congress to ameliorate conditions that constrain competitive market behavior in the generic specialty drug market.

THE ECONOMIC CAUSES OF CURRENT SHORTAGES IN GENERIC SPECIALTY DRUGS

Increased competition in the global generic drug industry favors firms' investment in newer drugs and decreases firms' ability to react to sudden changes in the cost of producing older drugs.

When making production decisions, firms weigh the expected revenues derived from the manufacturing of a generic molecule against the costs of producing that product. Revenue is a function of the quantity of the product the firm anticipates selling in the market and the prices that consumers of a given product will be willing to pay. Costs include the fixed costs of building, maintaining and staffing dedicated production facilities, the costs of meeting regulatory requirements for ensuring safety and product integrity, the variable costs entailed in the acquisition of component ingredients and the combination of these ingredients into finished products.

The generic pharmaceutical industry is a thin margin business which requires reliance on costly specialized equipment and labor, complex production processes and adherence to good manufacturing process regulations enforced by American and European Union regulatory authorities. Unlike the branded pharmaceutical market, in the generic market, intellectual property rights do not create temporary monopolies allowing firms to maintain high prices. Rather, the industry generates profits for their shareholders by investing in increasingly efficient production methods that optimize the short shelf life of the product, in effect, decreasing the costs of production. They also generate profits by choosing to invest in soon to be patent expired drugs that have demonstrated safety, efficacy and established demand in the market.

Furthermore, there has been considerable consolidation in this industry over the past decade; between branded and generic firms and among generic manufacturers. My preliminary research revealed sixteen out of the thirty-one cancer drugs in current short supply have been affected by industry consolidation; twenty-one of these drugs are currently manufactured by three or fewer independent firms. It is likely that consolidation in the industry has affected manufacturing capacity. Consolidations may result in plant closures or the repurposing of existing facilities for the production of other products. It is an open empirical question whether closures or repurposing of existing facilities have occurred in the manufacturing of generic infused specialty drugs. Increasing credit constraints existing across all capital-intensive industries could diminish global generic drug manufacturers' ability to react to sudden increases in the cost of production related to safety or other concerns. It is likely that increasing competition in the generic drug market has altered firm's investment decision-making. Firms must continuously weigh whether to continue to invest scarce resources in producing older generic drugs with limited demand or produce drugs with high demand soon to lose patent protection.

Finally, US regulation of the pharmaceutical industry commonly focuses exclusively on factors affecting demand and supply of these drugs in the domestic market. However, generic manufacturers of specialty drugs, including those in short supply, are multinational corporations that make investment decisions predicated on a global perspective. The international demand for access to effective drugs, has grown over time as the national incomes have increased in many developing nations (including Brazil, Russia, India and China). From the generic manufacturer's perspective, servicing these markets

is good business strategy. It is an open empirical question whether there are economies of scope that manufacturers can reap from the focused production of drugs servicing demand across markets. While there have been some sporadic reports of anticipated or temporary shortages of older generic specialty drugs in Canada and selected European Union countries, I am aware of no reported shortages among these drugs in China. My understanding is that provincial governments in these countries are willing to negotiate with manufacturers on price and quantity to satisfy the anticipated needs of their population.

In sum, it is likely that increasing competition in the global generic drug market has made the manufacturing of the older drugs in short supply less attractive than the production of newer therapies, where manufacturers can charge higher prices and sell more product in the domestic and international markets. Consolidation in this industry has likely reduced the manufacturing capacity of firms to make older generic drugs and their ability to adjust the supply of a product quickly if regulatory enforcement increases, safety concerns arise or other increases in the costs of production rise in their own plants or among their competitors. All of these forces act to limit the available quantity of older, generic specialty drugs and reduce the willingness of manufacturers to maintain production capacity to supply these drugs to the domestic market.

The organization of group purchasing arrangements is an important determinant of specialty drug availability.

Infused specialty drugs (and some oral chemotherapies) are purchased by health care providers. Generally, physician groups and hospitals do not directly purchase these drugs from manufacturers. Rather, distributers take physical possession of drugs from manufacturers and contracting groups negotiate the prices and quantity of bundles of products on behalf of their members. There are three different contracting channels in the US market: group purchasing organizations (GPO), secondary wholesalers, and government subsidized purchasers (including vendors servicing the 340B program for safety net providers).

I was unable to find empirical evidence on the percentage of sales by these channels among the drugs or drugs classes in current short supply. However, most reports suggest that the majority of physicians, hospitals and home health agencies belong to GPOs. GPOs consolidate demand for many different drug products. Since GPOs have consolidated purchasing power they are able to negotiate rebates and discounts off of list prices; some but not all of these price concessions are passed through to providers. Among providers that purchase drugs through a GPO there are variations in the amount of the discounted price and the preference for filling orders based on a provider's purchase volume. The GPO market has also consolidated in the past decade; many hospitals remain members of multiple GPOs.

Drugs can also be purchased through the secondary market. Generally, this market sells drugs to providers at less discounted prices that that offered through GPOs. However, recent reports suggest secondary dealers may provide lower prices for specialty infused drugs to community oncology groups than that offered by GPOs in selected geographical areas. There have also been reports of secondary market dealers offering limited quantities of the drugs in short supply at higher prices than that offered through GPOs, but this is likely a symptom and not a cause of such shortages. More empirical work is needed to understand the organization and pricing structure of the secondary market.

Government subsidized group purchasing organizations (including vendors servicing the 340B program) allow qualifying entities to purchase drugs from wholesalers at discounts of up to 50% off of list prices. Traditionally, entities have qualified for the 340B program based on their designation as a safety net hospital or clinic. In 2010, the program was expanded to include free standing cancer hospitals and other providers. While the overall scale of the program is likely to be small relative to the volume of sales of all specialty drugs, the numbers of providers that purchase drugs through the 340B program have quadrupled since 2005.

Not all parts of the country or all providers are equally affected by drug shortages. There is also variation in the geographical distribution of GPO membership and the importance of the 340B program to the provision of specialty care. Empirical evidence correlating purchasing channel membership strength and the presence and time frame of drug shortages is not available at this time. However, it is likely that low volume, community oncology practices are the least likely to be beneficiaries of preferential treatment in the GPO market. Therefore, these providers are the most likely to be vulnerable to interruptions in product supply, since purchasing arrangements reduce their access to the limited supply of these drugs, and also subject them to the highest prices.

The increased consolidation in the pharmaceutical industry diminishes the bargaining power of GPOs relative to that of manufacturers who sell a bundle of drugs. I expect consolidated manufacturers would prefer to sell drugs to GPOs with the highest revenue potential. This would again favor more commonly used drugs, with higher list prices, all else equal.

Furthermore, while there are limited penalties that work to compel generic manufacturers to produce an adequate supply of any drug, there are no penalties in place to compel generic manufacturers to maintain product reserves or excess capacity to produce therapy lines in case of domestic shortages or national emergency. GPO contracts typically include "failure to supply clauses". These provisions require manufacturers to reimburse the GPO for the price difference between the negotiated price and the purchased price, should the contracted manufacturer fail to supply product Yet they provide no reimbursement if there are no alternative sources for the drug, likely in the market for cancer drugs in short supply. These clauses also do not appear to prioritize medically necessary drugs or drug classes. Reports have suggested that the value of compensation required under these clauses has diminished over time. This is likely due to the increased bargaining power by manufacturers in this market, attained in part through consolidation.

In sum, empirical evidence regarding the nature of group purchasing of generic specialty drugs is limited. However, there is geographic and practice type variation in the presence of drug shortages. There is also variation in the distribution of GPO membership and the importance of the 340B program for the treatment of specialty medical conditions. Empirical evidence correlating purchasing channel membership strength and the presence and time frame of drug shortages is not available at this time. However, it is likely that low volume, community oncology practices are the least likely to be beneficiaries of preferential treatment in the GPO market. The consolidation of the generic pharmaceutical industry diminishes the bargaining power of purchasing channels to demand that certain drugs be included in the bundle. The consolidation also favors the sale of newer drugs with higher revenue potential for the manufacturers, and increases manufacturers ability to not satisfy existing "failure to supply" clauses.

Oncology practice culture and current Medicare reimbursement policy favors the use of new drugs.

Oncologists as agents for their patients determine the choice of treatment for a specific cancer. This choice is driven by physicians' attempts to maximize the health and well being of their patients. Adherence to current practice guidelines is an important aspect of treatment choice and a defining characteristic of the oncology profession. In the pharmaceutical market, there are few incentives to perform studies on the use of generic specialty drugs and limited incentives to perform head to head trials comparing older generic specialty drugs to newer branded treatments. Consequently, these factors favor physicians' choice of newer branded drugs with recently established safety and efficacy records.

In addition, oncologists are paid by insurers for the administration of chemotherapy and the "cost" of acquiring the drug. If the patient is insured under Medicare, these drugs are covered under the Medicare "Part B" program. Medicare is the largest insurer of cancer related treatment. It is an outstanding empirical question whether and how commercial insurers follow Medicare reimbursement practices for infused specialty drugs. Outpatient oncology practice revenues have been traditionally

tied to the difference between insurer reimbursement for infused specialty drugs and their wholesale acquisition cost (WAC) negotiated on their behalf by the above discussed purchasing channels. The difference is commonly called "cost recovery".

Reimbursement to physicians for the administration of "Part B" drugs by the Centers for Medicare and Medicaid has effectively declined over the past decade. In the early 1990s, Medicare Part B reimbursed physician-administered drugs at the Average Wholesale Price (AWP) listed in US Congress approved pricing compendia. AWP is essentially a suggested list price explicitly or implicitly set by manufacturers, which does not include rebates and discounts given to purchasers for volume, bundling or other rationales. The 2003 Medicare Modernization Act (MMA) switched the reimbursement benchmark for Part B drugs and biologics from AWP (or in some cases 95% of AWP) to 106% of the Average Sales Price (commonly referred to as "ASP+6%") effective on January 1, 2005. ASP represents the final price end users paid for each product averaged over most purchasers, reported directly to the CMS (Centers for Medicare and Medicaid) by each manufacturer starting in April 2004. Payments for existing drugs given to patients by physician practices in the outpatient setting were switched over to the ASP payment system with a two-quarter lag in January 2005. These reimbursement declines have put pressure on oncologists' practice revenues. It is likely these declines have negatively impacted the revenues of community oncologists more than oncologists practicing in high volume groups and locations. Empirical research suggests physicians change practice behavior based on changes to "Part B" drug reimbursement in order to maintain or increase practice revenue. It is likely these reimbursement changes reward the use of higher priced patent protected therapies that offer physicians higher "cost recovery".

Finally, private insurers in the primary care market have employed a number of policies to encourage the use of available generic therapeutic substitutes for the treatment of many prevalent chronic conditions. While some selected commercial insurers have recently begun to implement programs that encourage guideline consistent and cost effective treatment choices in the specialty setting; such policies have not been widely adopted by public payers.

In sum, oncology practice culture favors the use of newer chemotherapies with more recently established safety and efficacy data. Reimbursement to physicians for the administration of "Part B" drugs by the CMS has effectively declined over the past decade. Empirical research suggests physicians change practice behavior based on changes to "Part B" drug reimbursement in order to maintain or increase practice revenue. It is likely these reimbursement changes reward the use of higher priced patent protected therapies that offer physicians higher "cost recovery". The dominant payer in the specialty drug market (Medicare) has not adopted other policies promoting the use of generic therapies.

AN EVALUATION OF POTENTIAL POLICY RESPONSES TO REPORTED DOMESTIC SPECIALTY DRUG SHORTAGES

Numerous remedies have been proposed to ameliorate specialty drug shortages. I discuss the proposed tools at the disposal of Congress to ameliorate conditions constraining competitive market behavior in the generic specialty drug market.

Increase reimbursement to oncologists in the US to increase demand for drugs in short supply.

Proposals to increase physician payment include increasing ASPs for selected products, switching the reimbursement for selected short supply drugs from ASP to WAC, and/or decreasing the reimbursement adjustment lag for Medicare insured patients. All of these proposals are predicated upon the assumption that physicians will respond to increased payments for certain types of therapies and in turn "demand" more of these therapies for their practice use. Increased payment for certain drugs would reduce the strength of the incentive for physicians to prescribe the drug with the highest cost recovery for their practice, in effect equalizing the incentives to prescribe generic and branded

therapies for certain conditions. Presumably these demand side incentives would increase physicians' willingness and ability to pay for these selected drugs, which would be passed down to manufacturers. Manufacturers in turn could raise prices for these products to cover the additional expenses incurred in "meeting" demand.

Recent empirical work suggests physicians do appear to make prescribing decisions in part based upon variations and alterations in the reimbursement they receive from payers, holding patient benefit from a given therapy constant. However, empirical work in this area is in its infancy. It is unclear to me whether physicians will respond to increases in incentives to prescribe generic therapeutic substitutes in the same manner and magnitude as decreases in payment incentives that favor drugs with higher cost recovery for their practice. The strength of these reimbursement policies must be weighed against the importance of having oncologists adhere to currently available practice guidelines.

Second, WAC is considered by many health economists to more closely reflect the actual transaction prices that purchasers pay for patent protected drugs (including discounts and rebates) compared to ASP. Among patent protected drugs, WAC is approximately 20-30% higher than ASPs after accounting for the lag in reimbursement setting. From a policy makers perspective an evaluation of the merits of this proposal include the following: (1) Would increased payment to physicians be "passed" through the manufacturers and if so, in whole or in part?; (2) Would the switch from ASP+6% to WAC for drugs in short supply generate enough revenue for manufacturers to compensate for the increased costs incurred to produce more drugs; and (3) If an increased willingness and ability to pay for these drugs by providers generated a capacity building response by manufacturers, in what time frame would this response occur?

Regarding (1), there is limited empirical evidence to support (or deny) the proposition that providers would pass down the increased payment to manufacturers through existing contracting arrangements in whole or in part. The outcome largely depends upon the bargaining power of the manufacturer to wring higher prices from GPOs for these drugs. Markets with limited suppliers would likely have more bargaining power than those with significant generic entry and competition all else equal.

Regarding (2), there is very limited empirical evidence to support the assumption that the observed average patent protected drug WAC-ASP difference would carry over to the generic drug WAC-ASP difference. My research team's preliminary comparison of prices among the generic cancer drugs in short supply has not revealed a consistent difference in magnitude (or direction) between ASPs and WACs, consistent with results from a recent study by the Office of the Inspector General. In some cases, generic manufacturers do not report a WAC price; rather they negotiate prices on a maximum allowable cost model.

Regarding (3), there is limited evidence regarding the time frame in which generic manufacturers of specialty drugs in short supply could respond to the promise of anticipated revenues from increased willingness and ability to pay by providers (even if the increased payments were passed on from providers to manufacturers in lump sum). I expect the time frame varies considerably by manufacturer and by drug.

Eliminate programs that force significant price concessions from manufacturers and contribute to variation in practices experiencing drug shortages.

In theory, the elimination of the 340B program would directly act on the pricing of these drugs in the domestic market. The elimination of the program would eliminate the deep discounts for drugs that this program offers to some providers in the marketplace. This would in turn raise the reported ASP level for a variety of drugs over a short period of time across the entirety of the domestic market as 340B prices are incorporated into manufacturers' reported ASPs for each drug. The elimination of the program would also presumably force safety net providers to enter into more contracting with GPOs for "Part B" drug purchases and/or contracting with secondary wholesalers. While the consolidated

negotiating power of the GPOs and the secondary wholesalers would likely lower the acquisition prices previously obtained for some drugs; the prices would be partially offset by the increase in ASP derived from the elimination of the program.

However, the magnitude of these impacts, and consequently, their effect on ASP reimbursement rates is directly proportional to the relative importance of the 340 B market to the domestic market for these drugs overall and for the supply of local oncology markets. The volume and the prices of drugs in short supply purchased by 340B entities are open and important empirical questions as is the practice and geographical variation in the importance of the 340B program for drug purchasing. In the short term, the elimination of the program would likely aggravate shortages of some drugs among certain providers, since the elimination of the program would raise the effective prices they face for purchasing drugs. Exacerbating the issue, these providers are also likely the most credit constrained in the market for drugs. The acquisition of drugs across all therapeutic categories (including but not limited to those in current short supply) by these providers could be adversely affected. In my opinion, the elimination of this program alone, without coincident increases in providers' ability to pay for drugs and negotiate quantity commitments, would not strengthen vulnerable providers access to specialty drugs in short supply.

Levy penalties on generic manufacturers to ensure the supply of selected medically necessary drugs.

It has been suggested that penalties on generic manufacturers via purchaser channel contracts could be strengthened and targeted to apply to the supply of drugs or drug classes that are "medically necessary" for the treatment of American patients. A panel of medical experts would need to determine the inclusion criteria by therapeutic line and would also need to periodically update the list given the pace of innovation in the care of specialty medical conditions. For generic drug manufacturers a penalty for producing certain drugs would act to increase their production costs.

Generic drug manufacturers' compliance with these potential penalties are predicted upon (1) the magnitude and timing of the penalty and the strength of it's enforcement; and (2) the ability of the manufacturer to offset these increased production costs through the command of higher prices from purchasers. Given the bargaining power of the industry, due in part to consolidation, it is likely that manufacturers would be able to pass these costs off to purchasers. My examination of the generic manufacturers of oncology products in short supply suggests the majority of generic manufacturers produce multiple products across many therapeutic areas. These manufacturers are also multinational corporations. Consequently, it is an empirical question whether generic manufacturers would be able to either absorb these additional costs into the price setting of other generic drugs (mitigating their effect on the price setting for the drugs in short supply) and/or whether they would be able pass these higher costs of production onto all domestic and international purchasers of a given drug in short supply. Some observers have suggested increases in generic drug prices due to penalties would be offset by lower prices for patent protected drugs. There is no reason to expect this behavior; despite consolidation in the industry there remains considerable separation between multinational generic manufacturers and branded pharmaceutical firms.

CONCLUSION

Empirical research on the organization and financing of the generic supply of specialty drugs and the determinants of demand for these drugs by domestic and international markets is at its infancy. My assessment of the causes of current shortages suggest the highly competitive global nature of market competition in the supply of generic specialty drugs, firms limited excess capacity to produce these drugs, and their inability to react to sudden alterations in the cost of production for their own business or their competitors business are largely to blame for current shortages. Furthermore, the unique structure of the purchasing of these specialty drugs through multiple channels creates variation in the ability of providers to access the limited supply of these drugs at reasonable prices. Oncology practice culture favors the use of newer chemotherapies with more recently established safety and efficacy data.

Reimbursement to physicians for the administration of “Part B” drugs by the Centers for Medicare and Medicaid has effectively declined over the past decade. Empirical research suggests physicians change practice behavior based on changes to Part B drug reimbursement in order to maintain or increase practice revenue. It is likely these reimbursement changes reward the use of higher priced patent protected therapies that offer physicians higher “cost recovery”. The dominant payer in the specialty drug market (Medicare) has not adopted other policies promoting the use of generic specialty drugs. Numerous remedies have been proposed to ameliorate specialty drug shortages. They include: increasing reimbursement to oncologists in the US to increase demand for drugs in short supply, eliminating purchasing channels that force significant price concessions from manufacturers and aggravate geographic variations in drug shortage, and levying penalties on generic manufacturers to ensure the supply of selected medically necessary products in the domestic market. My evaluation of these proposals suggests each policy entails significant uncertainty regarding the intended and unintended consequences of their adoption. I do not believe the adoption of any one of these proposals is likely to substantially impact the supply of current drugs in short supply or alleviate the market conditions that may produce generic specialty drug shortages in the future.

Thank you.

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