Lost Prescription Drug Savings from Use of REMS Programs to Delay Generic Market Entry

BY ALEX BRILL

July 2014

MATRIX GLOBAL ADVISORS

EXECUTIVE SUMMARY

This study estimates the cost to U.S. health care payors of brand drug manufacturers' misuse of Risk Evaluation and Mitigation Strategies (REMS) and other restricted access programs. When brand manufacturers use these programs to withhold access to drug samples for generic manufacturers' bioequivalence testing and development, they can delay generic market entry and competition, thereby preserving high drug prices and preventing the cost savings generic drugs are known to deliver.

Nearly 40 percent of new FDA approvals are subject to REMS, and the percentage of REMS programs that require distribution restrictions has increased dramatically in the last several years. In addition, brand manufacturers have also begun imposing distribution restrictions on non-REMS products. As a result, government, consumers, and private payors are missing out on sizeable health care savings.

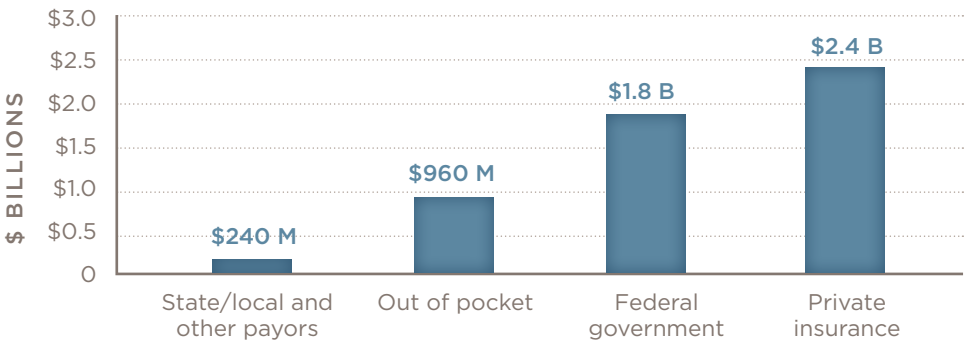
This paper estimates lost savings on forty generic small-molecule products whose market entry, according to a survey of generic drug manufacturers, is currently delayed by misuse of REMS or other restricted access programs. Specifically, this paper identifies $5.4 billion in annual pharmaceutical spending that could be saved if generic versions of the forty identified drugs were allowed to come to market. (See chart below.) This amount represents the annual lost savings for just those forty products included in this analysis; additional products continue to become subject to REMS programs on an ongoing basis.

An increase in brand drug companies' misuse of REMS and other restricted access programs is cause for concern. If this problem were to grow, the lost savings from delayed generic market entry would increase.

CASE STUDY: BIOLOGICS

Once the FDA provides final guidance on biosimilars, delaying biosimilar entry by restricting access to samples would result in approximately $140 million in lost savings for every $1 billion in biologics sales. This potential lost savings has enormous implications for the large and growing segment of pharmaceutical spending that biologics represent. Biologics accounted for 28 percent, or approximately $92 billion, of U.S. drug spending in 2013 — an increase of 9.6 percent since 2012.

$5.4 BILLION IN ANNUAL LOST SAVINGS FROM REMS MISUSE



Source: *MGA calculations based on IMS Health and National Health Expenditure data.*

INTRODUCTION

This study estimates the cost to U.S. health care payors of brand drug manufacturers' misuse of Risk Evaluation and Mitigation Strategies (REMS) and other restricted access programs. When brand manufacturers use these programs to withhold access to drug samples for generic manufacturers' bioequivalence testing and development, they can delay generic market entry and competition, thereby preserving high drug prices and preventing the cost savings generic drugs are known to deliver. Based on survey results from generic drug manufacturers, this study estimates the lost savings from this practice.

BACKGROUND

REMS programs are intended to improve drug safety for certain products by ensuring that the benefits for patients outweigh the risks. Toward this end, REMS programs require one or more of the following components: 1) medication guides; 2) communication plans; 3) "elements to assure safe use," which mandate various types of restrictions on product distribution; and 4) implementation systems, which can instruct manufacturers to monitor distribution and use.[1] The Food and Drug Administration Amendments Act of 2007 (FDAAA) granted the Food and Drug Administration (FDA) the authority to institute REMS programs for small-molecule drugs and biologics. Nearly 40 percent of new FDA approvals are subject to REMS, and brand companies have self-imposed non–FDA mandated restricted access programs on other products.[2] The FDA reports 70 currently approved REMS programs — 64 individual REMS and 6 shared system REMS.[3]

A shortcoming of REMS programs is the opportunity they afford brand drug manufacturers to thwart Abbreviated New Drug Application (ANDA) applicants' access to reference listed drugs. To receive FDA approval for an ANDA, a generic manufacturer must test the generic product it is developing against a sample of the brand drug to ensure bioequivalence. As the Federal Trade Commission (FTC) explains, "The unique regulatory framework that facilitates development and adoption of generic drugs depends on generic firms' ability to access samples of brand products."[4]

The FTC has expressed consternation over "the possibility that procedures intended to ensure the safe distribution of certain prescription drugs may be exploited by brand drug companies to thwart generic competition."[5] In fact, the risks are real. Our survey results indicate that brand manufacturers are indeed using REMS to deny generic manufacturers' access to brand drug samples.[6] Not only this, but brand manufacturers have also begun applying restricted access programs to drugs for which the FDA has not required a REMS program.[7]

Concerns about Consequences of REMS Misuse

If brand manufacturers can prevent generic companies from accessing their products, they succeed in protecting their market share, maintaining artificially high drug prices by keeping generic versions off the market. Preventing or delaying ANDA applicants' access to brand drugs for bioequivalence testing and development thus results in lost savings to consumers, private payors, and the federal government. Misuse of REMS and other restricted access programs has received attention on Capitol Hill, at the FTC, and even at the state level.

The House of Representative's first introduced version of the FDAAA (the 2007 legislation that authorized the FDA to use REMS programs) would have required brand drug manufacturers to sell a restricted access product at fair market value to a generic manufacturer for bioequivalence testing and development.[8] Several years later, the Senate-passed version of the Food and Drug Administration Safety and Innovation Act of 2012 would have required brand manufacturers to make samples of their products available to generic manufacturers for testing.[9] But neither the House nor the Senate provision survived to enactment.

In June 2014, the FTC cautioned, "If brand firms are able to block generic competition by denying access to the product samples needed to obtain FDA approval, this conduct may prevent the Hatch-Waxman framework from functioning as Congress intended."[10]

At the state level, Connecticut Attorney General George Jepsen has looked into REMS misuse, decrying the "disturbing, broader trend by certain branded drug manufacturers" to use restricted access "as a weapon to blunt the development of generic drugs."[11]

An increase in the existing use of REMS programs to block generic market entry is cause for concern. In recent years, "elements to assure safe use" — the component of REMS programs that mandates restricted distribution, and thus the primary component that brand manufacturers misuse — have become much more common. In 2009, only medication guides were required for roughly 75 percent of REMS programs, but now over 50 percent of REMS programs include elements to assure safe use.[12]

Missing thus far from the case against REMS misuse is a clear idea of the cost it imposes in terms of lost health care savings. This paper addresses this gap by estimating the lost savings from delayed generic market entry resulting from REMS misuse.

DATA AND METHODOLOGY

Using the following data and methodology, this paper analyzes generic products whose market entry is currently delayed by abuse of REMS and other restricted access programs and estimates how much could be saved if generic versions of these products were allowed to come to market.

Data

The products analyzed in this paper were identified by the Generic Pharmaceutical Association (GPhA) member companies who chose to participate in a survey conducted by Matrix Global Advisors (MGA). The survey was conducted from December 2013 to March 2014, and each company reported results confidentially. The reported products are brand drugs with REMS or other restricted access programs reportedly used to prevent generic manufacturers from accessing drug samples.

For each product with restricted access, MGA asked generic manufacturers to identify the product name, the brand manufacturer, whether the drug was small molecule or biologic, what strengths and dosage forms were restricted, the duration of the restriction, and whether the restriction was REMS-based or non-REMS. Eight companies participated in the survey.

After eliminating duplicates (i.e., products that more than one company reported), products for which sales data are not available through IMS Health, and products that were no longer restricted, we were left with forty small-molecule drugs in our analysis. According to generic manufacturers, brand drug companies currently use REMS programs to block generic access to 16 of these drugs and non-REMS restrictions to block access to the other 24 products.

For each of the forty identified drugs, we matched annual U.S. sales, utilization, and average prices from the IMS SMART Solutions database. Total U.S. sales for the forty small-molecule products analyzed here were approximately $7.6 billion in 2013 (annualized to account for some months of missing sales data). Among the brand drugs reported, the largest product had 2013 sales of roughly $1.5 billion, and the median product had 2013 sales of approximately $59 million.

The top four products constituted over 50 percent of sales. Our analysis also incorporated publicly available data from the National Health Expenditure Accounts on the breakdown of U.S. prescription drug spending by payor in 2012 (the latest year for which data are available).

Methodology

To model the lost savings from brand manufacturers' blocking generic access to these forty small-molecule products, we first determine the expected generic substitution rate — that is, the share of prescriptions that would be filled with a generic product if one were on the market. According to the IMS Institute for Healthcare Informatics, generics fill prescriptions 95 percent of the time when a generic is available.[13]

We next apply an estimate of the average price difference between brands and generics. According to the FDA, generic drugs are 80–85 percent cheaper than their brand counterparts.[14] The Congressional Budget Office (CBO), citing the National Association of Chain Drug Stores, pegs the average generic price discount at 75 percent.[15] In our model, we incorporate a 75 percent price discount, in the interest of deriving a conservative estimate of the lost savings from REMS misuse and to be consistent with CBO.

FIGURE 1. LOST SAVINGS CALCULATION

Annual savings from generic entry = [$ prior to generic entry] – [$ after generic entry]

= [(total Rx) * (brand price)] – [(brand Rx) * (brand price) + (generic Rx) * (generic price)]

= (total Rx) * (brand price) * (generic discount) * (generic substitution rate)

Using brand sales and utilization data from IMS for 2013 (the last full year for which data are available), we calculate lost savings by multiplying sales for each of the forty identified products by the average price discount (75 percent) and the average generic substitution rate (95 percent). It should be noted that the estimates of lost savings for these forty products are conservative because IMS data do not include all sales channels.

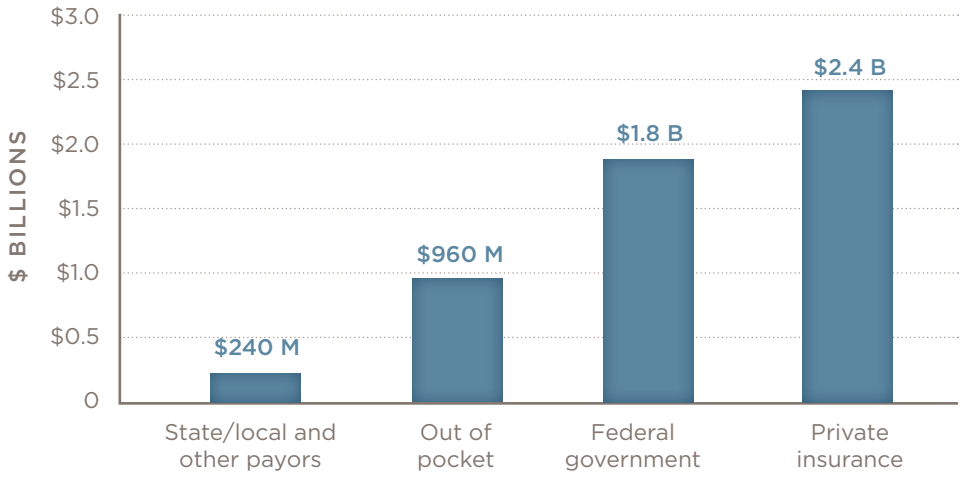
RESULTS

Based on observed pricing and utilization dynamics in the pharmaceutical industry and survey results of restricted access products, the economic cost of REMS misuse to delay generic market entry for these products totals $5.4 billion in lost savings to the U.S. health care system annually. The federal government bears a third of this burden, or $1.8 billion. Private insurance companies lose $2.4 billion, and consumers pay $960 million in extra out-of-pocket costs. State and local governments and other small payors lose savings of $240 million. (See **Chart 1**.)

Among government health care programs, Medicare, which accounts for nearly 26 percent of total U.S. prescription drug spending, experiences lost savings of $1.4 billion annually. The economic cost to Medicaid (both federal and state) totals $400 million.

In addition to being conservative (as explained above), these estimates should not be construed as the entirety of the lost savings from REMS misuse, either currently or going forward. First, not all currently restricted products are included in our analysis. And second, as the problem of brand drug companies' misuse of REMS and other restricted access programs grows, this lost savings will increase. On top of this, as the case study on the following page highlights, this issue can be expected to extend to biosimilars once the FDA provides final guidance for biosimilars to enter the market.

CHART 1. $5.4 BILLION IN ANNUAL LOST SAVINGS FROM REMS MISUSE



Source: *MGA calculations based on IMS Health and National Health Expenditure data.*

CASE STUDY: RESTRICTED ACCESS TO BIOLOGICS

In light of the forthcoming regulatory pathway for biosimilars and the pending patent cliff among biologics, access to biologic drugs for biosimilar approvals is critically important. In the current REMS environment, biologics makers will have the same opportunity to restrict access to samples of biologic drugs, with negative consequences to payors and patients.

Of the 64 currently approved individual REMS programs, 15 are for biologics. And generic manufacturers who responded to the survey on which the analysis in this paper is based reported restricted access to biologics samples already.

To capture the magnitude of the potential lost biosimilar savings from REMS misuse, we use the Congressional Budget Office's (CBO) assumptions about the market dynamics following biosimilar market entry. The competitive dynamics of the biologic drug market are not expected to mimic the dynamics in the small-molecule market. CBO expects an eventual 40 percent biosimilar price discount and 35 percent substitution rate.[1] This means that delayed biosimilar entry from restricted access would result in approximately $140 million in lost savings for every $1 billion in biologics sales ($1 billion * 40 percent * 35 percent).

This potential lost savings has enormous implications for the large and growing segment of pharmaceutical spending that biologics represent. Biologics accounted for 28 percent, or approximately $92 billion, of U.S. drug spending in 2013 — an increase of 9.6 percent since 2012.[2]

[1] Congressional Budget Office, cost estimate for S. 1695 Biologics Price Competition and Innovation Act of 2007, June 25, 2008.

[2] IMS Institute for Healthcare Informatics, "Medicine Use and Shifting Costs of Healthcare: A Review of the Use of Medicines in the United States in 2013," April 2014.

CONCLUSION

Nearly 40 percent of new FDA approvals are subject to REMS, and brand manufacturers have also begun imposing distribution restrictions on non-REMS products. Government, consumers, and private payors are already missing out on sizeable health care savings from misuse of these programs. Specifically, REMS and non-REMS strategies to restrict access to brand drug samples represent lost savings on small-molecule drugs of at least $5.4 billion annually. If REMS and non-REMS misuse were to grow, so too would the lost savings. In addition, if misuse were to extend to biologics when a biosimilars pathway is available, potential lost savings on biosimilars would be enormous. As this paper illustrates, curbing the misuse of REMS programs would yield demonstrable health care savings.

ABOUT THE AUTHOR

Alex Brill is the CEO of Matrix Global Advisors, an economic policy consulting firm. He is also a research fellow at the American Enterprise Institute and in 2010 served as an advisor to the Simpson-Bowles Commission. Previously, he was chief economist and policy director to the House Ways and Means Committee. Prior to his time on the Hill, he served on the staff of the President's Council of Economic Advisers.

This paper was sponsored by the Generic Pharmaceutical Association. The author is solely responsible for the content. Any views expressed here represent only the views of the author.

NOTES

[1] Food and Drug Administration (FDA), "Guidance for Industry: Format and Content of Proposed Risk Evaluation and Mitigation Strategies (REMS), REMS Assessments, and Proposed REMS Modifications," September 2009, available at www.fda.gov/downloads/Drugs/Guidances/UCM184128.pdf.

[2] Brief Amicus Curiae of Generic Pharmaceutical Association, Actelion Pharmaceuticals Ltd. v. Apotex Inc., (No. 1:12-cv-05743-NLH-AMD), (D.N.J. Mar. 2013), available at www.gphaonline.org/media/cms/GPhA_Amicus_Brief_filed_3_.pdf.

[3] FDA, "Approved Risk Evaluation and Mitigation Strategies (REMS)," available at www.fda.gov/drugs/drugsafety/postmarketdrugsafetyinformationforpatientsandproviders/ucm111350.htm (accessed May 28, 2014).

[4] Federal Trade Commission's Brief as Amicus Curiae, Actelion Pharmaceuticals Ltd. v. Apotex Inc., (No. 1:12-cv-05743-NLH-AMD), (D.N.J. Mar. 2013), available at www.ftc.gov/os/2013/03/130311actelionamicusbrief.pdf.

[5] Ibid.

[6] In addition to our survey results, others have written about REMS misuse. See, for example, Christopher Megaw, "Reviving Essential Facilities to Prevent REMS Abuses," *Columbia Journal of Law and Social Problems* 47, no. 2 (2013): 103–139.

[7] Generic manufacturers have privately reported restrictions on non-REMS products. In *Actelion Pharmaceuticals Ltd. v. Apotex Inc.,* the U.S. District Court for New Jersey examined the issue of brand manufacturers' blocking generic access to brand samples. One of the two products in question in *Actelion* was under a REMS program, but the other was not. Actelion, the brand manufacturer, articulated the rationale for restricting non-REMS products as well as REMS products thus: "Although Actelion's ability to sell samples . . . to the generics is constrained by the FDA-required distribution restrictions, Actelion's right to choose not to do business with potential rivals exists independently of those restrictions. Consequently, even if the generics could comply with such restrictions — *or if they did not exist* — Actelion is still under no legal duty to sell them samples." (Actelion Pharmaceuticals Ltd., Memorandum of Law in Support of Plaintiffs' Motion for Judgment on the Pleadings and to Dismiss Counterclaims, (D.N.J. Jan. 2012). Emphasis added.)

[8] Food and Drug Administration Amendments Act, H.R. 2900, 110th Congress, 1st session, introduced June 28, 2007.

[9] Food and Drug Administration Safety and Innovation Act, S. 3187, 112th Congress, 2d session, passed Senate May 24, 2012.

[10] Federal Trade Commission's Brief as Amicus Curiae, Mylan Pharmaceuticals, Inc. v. Celgene Corporation, (No. 2:14-CV-2094-ES-MAH), (D.N.J. Jun. 2014), available at www.ftc.gov/policy/advocacy/amicus-briefs/2014/06/mylan-pharmaceuticals-inc-v-celgene-corporation.

[11] Quoted in Dina ElBoghdady, "Generic-Drug Makers' Complaints over Brand-Name Access Prompt Investigations," *Washington Post*, May 22, 2012.

[12] Robert Maness and Brian Segers, "Refusal to Deal under FDA Imposed Risk Evaluation and Mitigation Strategies (REMS): Economic Considerations," *CPI Antitrust Chronicle* 4, no. 2 (Spring 2014), available at www.competitionpolicyinternational.com/refusal-to-deal-under-fda-imposed-risk-evaluation-and-mitigation-strategies-rems-economic-considerations.

[13] IMS Institute for Healthcare Informatics, "Medicine Use and Shifting Costs of Healthcare: A Review of the Use of Medicines in the United States in 2013," April 2014. The generic substitution rate varies by drug and may be higher or lower than the average rate (95 percent) for some drugs.

[14] FDA, "Facts about Generic Drugs," updated September 19, 2012, available at www.fda.gov/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/understandinggenericdrugs/ucm167991.htm.

[15] Congressional Budget Office, "Effects of Using Generic Drugs on Medicare's Prescription Drug Spending," September 2010, available at www.cbo.gov/sites/default/files/cbofiles/ftpdocs/118xx/doc11838/09-15-prescriptiondrugs.pdf.