REMS and Restricted Distribution Programs

AN ESTIMATE OF THE MARKET

By **Alex Brill** • June 2017

Executive Summary

The sustained concern over high drug prices has led policymakers to identify undue barriers to generic entry as a contributing factor. One such barrier is brand drug manufacturers' misuse of Risk Evaluation and Mitigation Strategy (REMS) and other restricted access programs to block generic competition. This study explains how REMS programs and other strategies are misused and estimates the parameters of the problem in terms of the number of drugs potentially affected and their total sales.

REMS programs are sometimes required by the Food and Drug Administration to help ensure the safety of certain prescription drugs. Depending on the level of risk associated with a product, a REMS program can require restricted distribution of a drug. But brand drug firms have been accused of using this requirement to deny generic manufacturers access to drug samples, which generic firms need for bioequivalence testing. Brand companies also self-impose restricted access programs on other products for the purpose of blocking access to drug samples.

There may of course be additional barriers to generic entry that generic manufacturers need to navigate, and not every restricted distribution program is necessarily used to block generic entry. But understanding the scale and scope of the restricted access drug segment offers a picture of the size of the potential problem.

The analysis presented in this study finds that the restricted access drug segment comprises 74 drugs with total sales of $22.7 billion in 2016:

- Forty-one of the drugs are restricted by REMS programs, with sales totaling $11.5 billion in 2016.
- The remaining 33 drugs are restricted by non-REMS programs, with total sales of $11.2 billion in 2016.
- Seven of the drugs (four restricted by REMS programs and three restricted by non-REMS programs) have sales over $1 billion; these seven drugs represent just over 50 percent of total sales.

Given the size and scope of the pharmaceutical market subject to a REMS or similar distribution restriction, this issue warrants attention on the scale of other high-priced drugs that have generated headlines and Congressional inquiries. There are valid public health reasons for restricted access programs for certain drugs, but misuse of these programs to block generic competition has a direct negative impact on consumers and taxpayers.

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Introduction

High drug prices remain a concern among policymakers, and while a number of factors have been identified as causes, undue barriers to generic entry is one that has recently garnered increased attention. One proposed solution is legislation to stop brand drug companies from improperly using Risk Evaluation and Mitigation Strategy (REMS) programs and other restricted access programs to block generic competition. This study explains how REMS programs and related strategies are misused and estimates the parameters of the problem in terms of the number of drugs potentially affected and their total sales. Given the size and scope of the pharmaceutical market subject to a REMS or similar distribution restriction, this issue warrants attention on the scale of other high-priced drugs that have generated headlines and Congressional inquiries.

Background

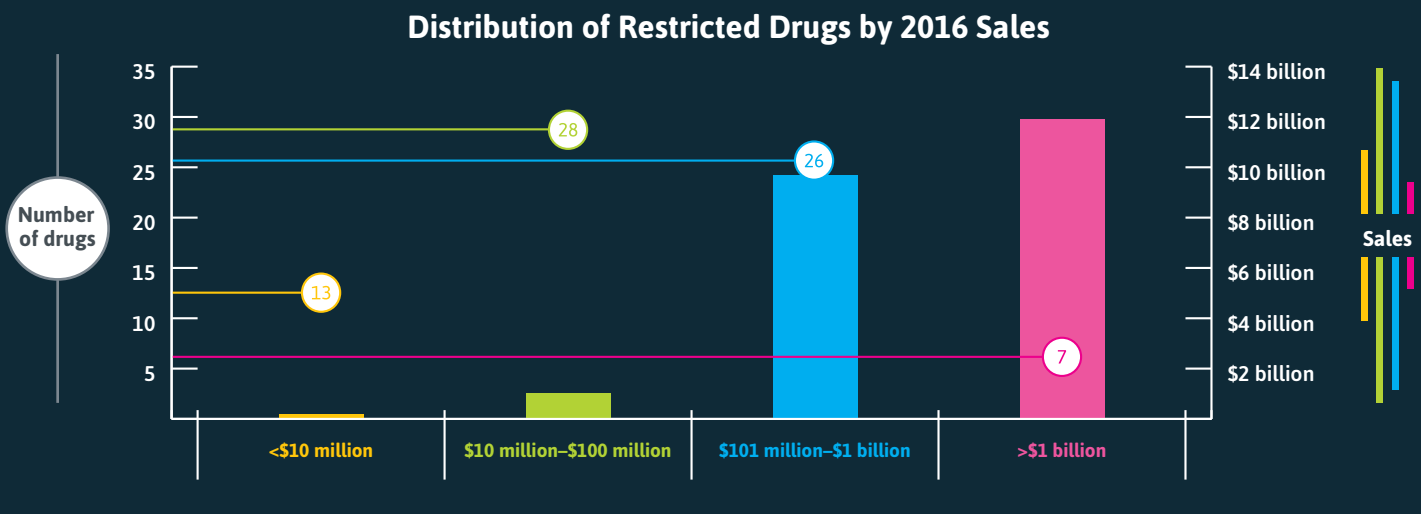
REMS programs are sometimes required by the Food and Drug Administration (FDA) to help ensure the safety of certain small-molecule drugs and biologics. Depending on the level of risk associated with a product, a REMS program can require one or more of the following: a medication guide; a communication plan; "elements to assure safe use" (ETASU), which mandate various types of restrictions on product distribution; and an implementation system, which can instruct manufacturers to monitor distribution and use. Nearly 40 percent of new FDA approvals are subject to REMS programs.[1] There are currently 71 REMS programs in place, and 42 of them include ETASU[2] – the restricted distribution component that brand drug companies can use to hinder generic drug manufacturers' attempts to bring competitor products to market.

In order to receive FDA approval for a generic product in development, a generic manufacturer must test the product against a sample of the brand drug to ensure bioequivalence. But brand drug firms have been accused of using REMS programs with ETASU to deny access to drug samples requested by generic firms. On top of this, brand companies self-impose restricted access programs on other products for the purpose of blocking access to drug samples. REMS programs with ETASU have become much more common in recent years. In 2009, only medication guides were required for roughly 75 percent of REMS programs, but now nearly 60 percent of REMS programs include ETASU. And the use of REMS-like programs to block generic market entry has also been on the rise.

If brand manufacturers stop generic companies from accessing samples, they can effectively keep a generic off the market, thus protecting their monopoly market position and denying price competition. This practice can result in substantial lost savings to consumers and private and public payors, as generic drugs are on average 80–85 percent cheaper than their brand counterparts.[3] In 2014, I analyzed 40 drugs for which brand companies were refusing to provide samples, as reported by generic manufacturers. I estimated that $5.4 billion in annual drug spending could be saved if generic versions of these drugs came to market.[4]

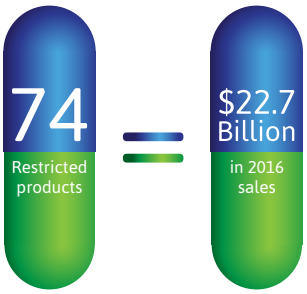
Since the Food and Drug Administration Amendments Act of 2007 (FDAAA) allowed the FDA to institute REMS programs, there has been concern about the potential for misuse. In fact, the first version of the FDAAA introduced in the House of Representatives included a provision that would have required brand drug manufacturers to sell a restricted access product at fair market value to a generic manufacturer for bioequivalence testing and development.[5] But this provision was not retained in the final bill.

Over the last decade, as these concerns have been borne out, the FDA and the Federal Trade Commission alike have expressed the need to address the misuse of REMS and other restricted access programs. Lawmakers on Capitol Hill have attempted to enact legislation correcting the problem, but so far without success.The most recent legislative attempts include two bipartisan bills introduced in April 2017, the Creating and Restoring Equal Access to Equivalent Samples Act (known as the CREATES Act) and the Fair Access for Safe and Timely Generics Act (or the FAST Generics Act).



Scale and Scope of Restricted Access Drug Segment

To determine the scale and scope of this problem, I estimate the size of the brand drug market that is currently restricted due to REMS with ETASU or other restricted distribution programs used by brand drug companies to prevent generic competition. There may of course be additional barriers to generic entry that manufacturers need to navigate with respect to any particular generic application, and certainly not every restricted distribution program (REMS with ETASU or otherwise) is necessarily used to limit generic entry. However, the number of brand drugs and the size of the affected markets offer a picture of the size of the potential problem posed by the misuse of these programs.



For this analysis, I examine all brand drugs under REMS programs with ETASU,[6] excluding those products for which a generic is already approved.[7] I also look at brand drugs identified by generic drug manufacturers as restricted under non-REMS programs. These drugs were identified in a survey that the Association for Accessible Medicines conducted of its members. Before including a non-REMS drug in the analysis, I ascertained that there was no approved generic version in the FDA Orange Book.[8]

The analysis consists of 41 products under REMS programs with ETASU with sales totaling $11.5 billion in 2016, and 33 non-REMS restricted products with total sales of $11.2 billion in 2016.[9] The combined size of the restricted access drug segment is thus 74 drugs with total sales in 2016 of $22.7 billion. Sales for these drugs in 2016 averaged $307 million. Seven of the drugs had sales over $1 billion, and these seven represent just over 50 percent of total sales. Four of the seven (Revlimid, Suboxone, Tysabri, and Truvada) are under REMS programs with ETASU, and the other three (Aubagio, Imbruvica, and Zytiga) were identified by surveyed generic firms as restricted by a non-REMS program.

High-Profile, High-Price Drugs

Considering the size of the restricted access drug segment – $22.7 billion in sales in 2016 – relatively little public attention has been given to it. For context, it is helpful to compare it to high-priced products that have generated attention-grabbing headlines and widespread outrage.

For example, Sovaldi, the hepatitis C drug that made headlines in 2014 with a price of $1,000 a pill, had 2016 sales of $2.4 billion. Daraprim – the drug that made Martin Shkreli infamous in 2015 when his company, Turing Pharmaceuticals, purchased it and raised the price 5,000 percent – had 2016 sales of $19 million. And the heart drugs Isuprel and Nitropress – two of the products over which Valeant Pharmaceuticals took heat in 2015 for exorbitant price increases – had 2016 sales of $400 million.[10]

Of course, these are anecdotes that highlight broader public policy concerns about high drug prices, but they do offer helpful context for the drug segment subject to restricted access programs.

Conclusion

There are valid public health reasons for restricted access programs for certain drugs, but brand manufacturers can use these programs to block generic competition. This has a direct negative impact on consumers and taxpayers, but it is not widely understood. Compared to the size of other prescription drugs that have generated policymaker and public ire, the potential for misuse of REMS and other restricted access programs is substantial.

Notes

[1] 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.

[2] Food and Drug Administration (FDA), "Approved Risk Evaluation and Mitigation Strategies (REMS)," available at www.accessdata.fda.gov/scripts/cder/rems (accessed May 19, 2017).

[3] FDA, "Facts about Generic Drugs," updated June 28, 2016, available at www.fda.gov/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/understandinggenericdrugs/ucm167991.htm.

[4] Alex Brill, "Lost Prescription Drug Savings from Use of REMS Programs to Delay Generic Market Entry," Matrix Global Advisors, July 2014, available at www.getmga.com/wp-content/uploads/2017/02/REMS_Study_July.pdf.

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

[6] FDA, "Approved Risk Evaluation and Mitigation Strategies (REMS)," available at www.accessdata.fda.gov/scripts/cder/rems (accessed May 19, 2017).

[7] As mentioned above, there are 42 REMS programs with ETASU, some of which apply to more than one drug. Excluding products that have already gone generic leaves 50 drugs under REMS programs with ETASU. However, 9 of these drugs do not have sales data for 2016 in the QuintilesIMS SMART Solutions database. This portion of the analysis is based on the remaining 41 products.

[8] Brand drugs not under a REMS program but for which samples are reportedly being denied total 37, but 4 do not have sales data for 2016 in the QuintilesIMS SMART Solutions database. This portion of the analysis is based on the remaining 33 products.

[9] All sales data derived from the QuintilesIMS SMART Solutions database.

[10] Sales data for Daraprim, Isuprel, Nitropress, and Sovaldi derived from the QuintilesIMS SMART Solutions database.

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.

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