Effect of Generic Competition on Atorvastatin Prescribing and Patients’ Out-of-Pocket Spending

Jing Luo, MD, MPH; John D. Seeger, PharmD, DrPH; Macarius Donneyong, PhD; Joshua J. Gagne, PharmD, ScD; Jerry Avorn, MD; Aaron S. Kesselheim, MD, JD, MPH

IMPORTANCE In November 2011, the cholesterol level-lowering medication atorvastatin calcium became available in the United States as a generic drug. However, only a single generic form (from a manufacturer that qualified for market exclusivity by challenging several of Pfizer’s patents) and an authorized generic form (a brand-name drug sold as a generic) were available for the first 180 days.

OBJECTIVE To describe trends in the prescribing of generic atorvastatin after expiration of market exclusivity for the brand-name medication and the effect on patients’ out-of-pocket spending.

DESIGN, SETTING, AND PARTICIPANTS A US population-based study used commercial claims data from the Optum Clinformatics research database (UnitedHealth Group) from December 1, 2010, to May 31, 2013. Participants were 1,968,709 adults with commercial insurance who had been prescribed 1 or more statins (13,285,223 statin prescriptions). An interrupted times series model was used to examine the effect of limited and full generic competition on brand-name and generic atorvastatin prescriptions. Data were analyzed from December 1, 2010, to May 31, 2013.

EXPOSURES Prescription of brand-name atorvastatin, generic atorvastatin, and authorized generic atorvastatin were distinguished using National Drug Codes.

MAIN OUTCOMES AND MEASURES Total number of prescriptions dispensed per month and out-of-pocket expenditures for a typical 30-day supply of 20-mg atorvastatin during the periods of brand-name availability only, limited generic competition (lasting 180 days after market exclusivity ended), and full generic competition.

RESULTS Of the 1,968,709 beneficiaries, 1,483,066 (58.8% male and 41.2% female; mean [SD] age, 55.6 [10.2] years) received a prescription for a single statin and were included in the analysis. The introduction of the first generic competitor was associated with a reduction in monthly brand-name atorvastatin fills by 20,896 prescriptions (level change, \( P = .001 \)), an 18.1% change compared with the month preceding loss of exclusivity. Full generic competition reduced brand-name fills by 54,944 prescriptions (level change, \( P < .001 \)), a 47.6% change relative to the month preceding loss of exclusivity. During the first 180 days of generic competition, no meaningful difference in monthly out-of-pocket spending was found between brand-name (median, $16.98; interquartile range [IQR], $8.76-$48.66) and generic (median, $19.98; IQR, $7.50-$54.90) atorvastatin. After full generic competition, estimated monthly out-of-pocket spending for generic atorvastatin (median $5.10; IQR, $3.36-$19.98) or authorized generic atorvastatin (median, $5.52; IQR, $3.48-$19.98) was substantially lower than that for brand-name atorvastatin (median, $30.00; IQR, $15.00-$91.38).

CONCLUSIONS AND RELEVANCE Among patients with commercial health insurance, delays in generic uptake and high levels of out-of-pocket spending during the first 180 days after atorvastatin lost market exclusivity slowed changes in drug prescribing and decreases in patients’ out-of-pocket costs.
Originally approved in 1996, atorvastatin calcium (Lipitor) marketed by Pfizer was the top-selling prescription drug in the United States from 2007 to 2011, with annual sales of greater than $7 billion.1 During those years, atorvastatin represented approximately one-quarter of all prescribed medications in the class of cholesterol level-lowering hydroxymethyl glutation coenzyme A reductase inhibitor (statin) drugs, second only to simvastatin (Zocor), which was available as a generic drug during that time and accounted for approximately 40% of statin sales.2 In late 2011, generic versions of atorvastatin started to reach the market.

Physicians and the public often assume that once a brand-name drug loses patent protection, a number of different generic manufacturers receive marketing approval by the US Food and Drug Administration (FDA) to sell less expensive but chemically and clinically interchangeable versions of the brand-name drug. However, atorvastatin’s transition from brand-name–only availability to a competitive generic market occurred slowly for several reasons. First, the date of generic entry was delayed. An Indian drug manufacturer, Ranbaxy (now Sun Pharmaceutical), was the first company to file an application with the FDA seeking marketing approval for a generic version of atorvastatin. Ranbaxy’s generic product could have occurred slowly for several reasons. First, the date of generic entry was delayed. An Indian drug manufacturer, Ranbaxy (now Sun Pharmaceutical), was the first company to file an application with the FDA seeking marketing approval for a generic version of atorvastatin. Ranbaxy’s generic product could have launched as early as March 2010 but litigation over Pfizer’s patent on atorvastatin, full generic competition did not occur immediately. The 1984 Hatch-Waxman Act amendments to the Food, Drug and Cosmetic Act4 included a pathway that provides 180 days of generic marketing exclusivity to the first generic manufacturer challenging a potentially invalid pharmaceutical patent. During this period, the FDA cannot approve applications seeking marketing authorization for a generic submitted by other manufacturers. Because Ranbaxy qualified for the 180-day period by challenging several of Pfizer’s unexpired patents on atorvastatin, full generic competition did not occur until May 2012, when 4 other manufacturers received FDA approval to market their versions.

To further protect its revenue, Pfizer introduced an “authorized generic” of the drug (made by Watson, under license from Pfizer) at the same time as Ranbaxy’s version. An authorized generic is a brand-name product sold under a generic name. Pfizer also attempted to maintain market share by aggressively negotiating discounts or rebates with health plans and pharmacy benefit managers in exchange for preferred formulary status or exclusive rights to mail-order services. In December 2010, Pfizer also launched a $4 copayment coupon to steer patients away from generic competitors.2,5,6 We herein analyze the effect of Ranbaxy’s 180-day marketing exclusivity period and Pfizer’s introduction of an authorized generic on patterns of atorvastatin use and out-of-pocket costs for patients with commercial health insurance.

Methods

Data Source and Patient Population

We extracted population-level data on prevalent statin use from the Optum Clinformatics research database, which covers 14 million current beneficiaries insured under UnitedHealth Group.7–10 Eligible patients were 18 years or older, had at least 180 days of continuous enrollment, and had filled a prescription for at least 1 statin (atorvastatin, simvastatin, rosuvastatin, fluvastatin, pitavastatin, lovastatin, pravastatin, combined amiodipine besylate and atorvastatin, combined ezetimibe and simvastatin, combined atorvastatin and ezetimibe, combined niacin and simvastatin, or combined niacin and lovastatin) from December 1, 2010 (1 calendar year before the first generic entry), to May 31, 2013 (1 calendar year after full generic competition). This study was approved by the institutional review board of Brigham and Women’s Hospital and Harvard Medical School, which waived the need for informed consent for the deidentified patient data.

We identified patient and prescription counts of prevalent statin users. We classified atorvastatin users into 1 of the following 3 categories using the FDA’s National Drug Code: (1) brand-name atorvastatin (Pfizer), (2) generic atorvastatin (various manufacturers), and (3) authorized generic atorvastatin (Watson). We used a cross-walk file to convert the 11-digit billing codes available in Optum to the FDA’s 10-digit National Drug Code.11

We used claims-based definitions from the International Classification of Diseases, Ninth Revision, and a comorbidity score (eTable in the Supplement) to assess demographic and clinical characteristics of prevalent users.12 We assessed for clinical characteristics during the 180 days before each patient’s index prescription.

Study Interventions

We divided our 30-month study into 3 time segments using 2 policy interventions. The first segment (market exclusivity) ended on December 1, 2011, 1 day after Ranbaxy’s first generic atorvastatin entered the market. The second segment (limited generic competition) continued until May 31, 2012, 3 days after the end of Ranbaxy’s 180-day generic marketing exclusivity period. The third segment (full generic competition) started on June 1, 2012, and continued until the end of the study period. The authorized generic version was available during the limited and full generic competition segments. A very small number of prescription fills were misclassified because of the way we defined our interventions. For example, during the final month of market exclusivity, November 2011, 379 prescriptions (<0.33% of brand-name atorvastatin fills) for authorized generic atorvastatin were filled but not included as data points in our segmented
regression analysis because the start of the first policy intervention (limited generic competition) was set on December 1, 2011.

Outcome Measures
The primary outcome consisted of prescriptions of brand-name, generic, and authorized generic atorvastatin (total number of dispensed prescriptions per month). Our secondary outcome was out-of-pocket spending (defined as the sum of the beneficiary copayment and deductible amounts). We determined the out-of-pocket spending per milligram of dispensed drug by dividing the out-of-pocket amount by the product of the quantity supplied and dosage strength. In contrast to previous reports examining cost outcomes from generic entry using retail or average wholesale prices,13,14 out-of-pocket spending better reflects real costs to patients because few pay the full retail price. We then multiplied the median and 25th and 75th percentiles of spending per milligram of dispensed drug for each segment by the most common strength (20 mg) and days supplied (30 days).

Statistical Analysis
Data were analyzed from December 1, 2010, to May 31, 2013. We used interrupted time series models to evaluate the longitudinal effect of limited and full generic competition on atorvastatin use. Segmented regression analysis of time series data has been previously described in pharmaceutical research and allows one to determine whether observed changes in the level or the trend of prescription drug dispensations should be attributed to a policy intervention or to chance alone.16 We created indicators for each time segment and an indicator for calendar month and then used these indicators in a linear regression model to predict use of brand-name, generic, and authorized generic atorvastatin. For the latter 2 outcomes, we used a model that began on the first intervention. We adjusted for first-order and higher-order autocorrelation of error terms using PROC AUTOREG in SAS statistical software (version 9.4; SAS Institute Inc) with a lag of up to 12 months. We tested for serial first-order and higher-order autocorrelation of error terms using the Durbin-Watson statistic. All analyses were conducted on SAS statistical software. We considered P values of less than .05 as statistically significant.

Results
Patient Characteristics
Our analytic cohort included 1 968 709 beneficiaries who filled 13 285 223 statin prescriptions during the study period. After excluding those who had fills for more than 1 type of statin (n = 485 643), our cohort included 1 483 066 individuals (58.8% male and 41.2% female; mean [SD] age, 55.6 [10.2] years). Their characteristics are shown in Table 1. Of these, 12.9% had a diagnosis of coronary artery disease or ischemic heart disease during the covariate assessment period, suggesting that most received statins for primary prevention of cardiovascular disease.

Atorvastatin Use
Part A of the Figure shows the change in levels and trends of monthly brand-name atorvastatin prescriptions during the study period. A level change refers to an increase or decrease in the number of prescription fills after the intervention (limited generic competition or full generic competition). A trend change refers to an increase or decrease in the slope of the segment after the intervention compared with the segment preceding the intervention. Limited generic competition was associated with a reduction in monthly brand-name atorvastatin fills of 20 896 prescriptions (level change, P = .001), an 18.1% change compared with the month preceding loss of exclusivity. In the next 6 months, brand-name atorvastatin prescriptions declined by 1346 prescriptions per month, although the difference was not significant compared with the numbers during the baseline segment (P = .33).

Full generic competition was associated with a reduction in monthly brand-name atorvastatin fills of 54 944 (level change, P < .001), a 47.6% change relative to the month preceding loss of exclusivity. Subsequently, the rate of prescription fills further declined by 3006 prescriptions per month.

### Table 1. Characteristics of the Patients in the Study Cohort Who Filled Prescriptions for Statins During the Study Perioda

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. (%) of Patients (n = 1 483 066)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>871 771 (58.8)</td>
</tr>
<tr>
<td>Female</td>
<td>611 295 (41.2)</td>
</tr>
<tr>
<td>US region</td>
<td></td>
</tr>
<tr>
<td>Northeast</td>
<td>133 145 (9.0)</td>
</tr>
<tr>
<td>South</td>
<td>732 443 (49.4)</td>
</tr>
<tr>
<td>Midwest</td>
<td>393 090 (26.5)</td>
</tr>
<tr>
<td>West</td>
<td>224 388 (15.1)</td>
</tr>
<tr>
<td>Insurance plan</td>
<td></td>
</tr>
<tr>
<td>HMO</td>
<td>132 062 (8.9)</td>
</tr>
<tr>
<td>PPO</td>
<td>55 479 (3.7)</td>
</tr>
<tr>
<td>Other</td>
<td>1 295 525 (87.4)</td>
</tr>
<tr>
<td>Prior myocardial infarction</td>
<td>35 407 (2.4)</td>
</tr>
<tr>
<td>Hyperlipidemia and/or hypercholesterolemia</td>
<td>1 025 682 (69.2)</td>
</tr>
<tr>
<td>Hypertriglyceridemia</td>
<td>24 065 (1.6)</td>
</tr>
<tr>
<td>Coronary artery disease and/or ischemic heart disease</td>
<td>191 688 (12.9)</td>
</tr>
<tr>
<td>Family history of ischemic heart disease</td>
<td>14 026 (0.9)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>746 336 (50.3)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>371 967 (25.1)</td>
</tr>
<tr>
<td>Obesity</td>
<td>94 026 (6.3)</td>
</tr>
<tr>
<td>Smoking</td>
<td>72 598 (5.0)</td>
</tr>
<tr>
<td>Stroke or TIA</td>
<td>34 984 (2.4)</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>55.6 (10.2)</td>
</tr>
<tr>
<td>No. of unique medications, mean (SD)b</td>
<td>6.09 (4.1)</td>
</tr>
<tr>
<td>No. of hospitalizations 180 d before the index prescription, mean (SD)</td>
<td>1.17 (0.6)</td>
</tr>
<tr>
<td>Gagne combined comorbidity score, mean (SD)c</td>
<td>0.01 (0.3)</td>
</tr>
</tbody>
</table>

Abbreviations: HMO, health maintenance organization; PPO, preferred provider organization; TIA, transient ischemic attack.

b Determined for each beneficiary by examining their prescription drug history 180 days before receipt of their index statin prescription.
c This score predicts 1-year mortality and was developed by combining measures from the Charlson and Elixhauser measures. Scores range from −2 to 26, with greater numbers indicating more comorbidities.
Methods section).

Regression model (described in the Statistical Analysis subsection of the Methods section).

atorvastatin, which we refer to as the start of limited generic competition.

December 1, 2011, indicates the end of market exclusivity for brand-name atorvastatin. Predicted monthly prescription fills are calculated from the linear regression model (described in the Statistical Analysis subsection of the Methods section).

Data are shown for December 2, 2010, to May 31, 2013. The vertical bar at December 1, 2011, indicates the end of market exclusivity for brand-name atorvastatin, which we refer to as the start of limited generic competition. The vertical bar at June 1, 2012, indicates the start of full generic competition. Predicted monthly prescription fills are calculated from the linear regression model (described in the Statistical Analysis subsection of the Methods section).

(trend change compared with the segment of limited generic competition, $P = .04$).

The first month of full generic competition was associated with an increase in prescription fills for generic atorvastatin (Figure, B) of 40,037 (level change, $P < .001$). Subsequently, the trends in the rate of prescriptions during the segment of full generic competition and the segment of limited generic competition were similar ($P = .63$).

Full generic competition was associated with an increase of authorized generic prescriptions (Figure, C) of 23,367 per month (level change, $P = .002$). During the segment of limited generic competition, use of authorized generic atorvastatin decreased by 121 prescriptions per month. After full generic competition, use of authorized generic atorvastatin increased by 1201 prescriptions per month; however, the trend change comparing this segment with the segment of limited generic competition was not significant ($P = .48$) (Table 2).

We conducted sensitivity analysis to examine whether any underlying trends or monthly or seasonal variation in statin use or hyperlipidemia diagnoses were found in the Optum Clininformatics research database. No apparent trends needed to be accounted for in our analysis.

### Atorvastatin Spending

Total out-of-pocket expenditures for brand-name atorvastatin ranged from a high of $5.41 million in January 2011 to a low of $161,000 in May 2013. By contrast, out-of-pocket expenditures for generic atorvastatin started at $1.04 million in December 2011 and peaked at $1.96 million in January 2013 before falling to $1.75 million in May 2013.

Table 3 summarizes the estimated out-of-pocket spending for a 30-day supply of the most common formulation (20 mg) of brand-name, authorized generic, and other generic atorvastatins during the 3 study segments. During the market exclusivity segment, the median monthly out-of-pocket spending was $17.50 (interquartile range [IQR], $10.02-$49.98). During limited generic competition, out-of-pocket spending for brand-name atorvastatin (median, $16.98; IQR, $8.76-$48.66) was similar to spending for the authorized generic (median, $19.98; IQR, $7.50-$54.90) and Ranbaxy’s generic (median, $17.70; IQR, $4.98-$51.48) atorvastatin. During full generic competition, out-of-pocket spending for brand-name atorvastatin (median, $91.38) was substantially higher than spending for the authorized generic (median, $30.00; IQR, $3.48-$19.98) or the other generic (median, $5.10; IQR, $3.36-$19.98) atorvastatins.

### Discussion

After expiration of market exclusivity for atorvastatin, the top-selling drug in the United States for 4 years, we examined prescription and spending data from a large commercial health insurance company. Using segmented regression methods, we found that prescription fills for brand-name atorvastatin only decreased slightly in the first 6 months, which included the introduction of a single generic and an authorized generic product. After full generic competition was permitted, brand-name atorvastatin fills decreased substantially, with an inflection point

Data are shown for December 2, 2010, to May 31, 2013. The vertical bar at December 1, 2011, indicates the end of market exclusivity for brand-name atorvastatin, which we refer to as the start of limited generic competition. The vertical bar at June 1, 2012, indicates the start of full generic competition. Predicted monthly prescription fills are calculated from the linear regression model (described in the Statistical Analysis subsection of the Methods section).
occurred approximately 7 months after loss of exclusivity. During the segment of limited generic competition, out-of-pocket costs did not substantially differ for brand-name, authorized generic, and generic atorvastatin. After full generic competition, out-of-pocket costs were substantially lower for the generic drugs.

The end of a drug’s patent exclusivity does not necessarily lead to immediate, substantial changes in patients’ out-of-pocket spending. Prior studies have characterized the market dynamics accompanying loss of marketing exclusivity for prescription drugs, showing that overall drug prices and brand-name market share tend to decrease with an increasing number of generic competitors. Such outcomes, however, can be delayed owing to the 180-day generic marketing exclusivity period and the introduction of authorized generic drugs, as was the case with atorvastatin. Delays in the availability of generic versions may be important because brand-name Lipitor has not been shown to be clinically superior to generic atorvastatin. On the contrary, in part because of the lower cost of generic statins, patients initiating therapy to lower lipid levels with these products have better adherence and lower risk for hospitalization and death than patients initiating therapy with brand-name statins.

When the 180-day generic exclusivity period was conceived, the goal was to provide incentives to generic competitors to challenge potentially invalid patents protecting brand-name products. In 1984, such a provision was useful to help stimulate the relatively small generic drug market. In recent years, however, many questionable brand-name patents have remained in effect because of litigation settlements between brand-name and generic companies. Such settlements can be in the financial interests of brand-name and generic manufacturers, but not of patients, because they allow patents to persist that might have been overturned. The 180-day period can even hinder generic competition. For the blood pressure drug valsartan (Diovan), the company holding the 180-day market exclusivity did not initially receive FDA approval to launch its generic version, in part owing to manufacturing deficiencies. The course of events led to a 20-month delay in generic competition that effectively prolonged exclusivity for the brand-name version; the manufacturer valued the extra sales at $100 million per month.

Authorized generic drugs might be viewed as a net benefit for consumers by offering a lower-cost option than the brand-name version. A 2011 report from the Federal Trade Commission found that entry of authorized generics slightly lowered generic drug prices, although we found no difference in patients’ out-of-pocket costs. The Federal Trade Commission also concluded that brand-name manufacturers launch authorized generics to capture revenue from the first generic challenger during the 180-day generic exclusivity period, which could reduce in the long term the incentive for generic firms to establish new generic entry.

### Table 2. Changes in Level and Monthly Trends in Filled Prescriptions for Brand-Name and Generic Atorvastatin, 2010-2013

<table>
<thead>
<tr>
<th>Atorvastatin Prescription</th>
<th>Effect Estimate (SE)*</th>
<th>Limited Generic Competition</th>
<th>Full Generic Competition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Market Exclusivity</td>
<td>P Value</td>
<td>P Value</td>
</tr>
<tr>
<td>Brand-name</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level</td>
<td>NA</td>
<td>NA</td>
<td>−20,896 (5800)</td>
</tr>
<tr>
<td>Trend</td>
<td>NA</td>
<td>NA</td>
<td>−1346 (1363)</td>
</tr>
<tr>
<td>Generic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Trend</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Authorized generic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Trend</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

**Abbreviation:** NA, not applicable.

*Effect estimates refer to a change in the number of prescription fills per month (level) or a change in the slope of a regression line (trend) for the associated segment and are calculated from the segmented regression analysis. Market exclusivity lasted from December 1, 2010, to November 30, 2011; limited generic competition, from December 1, 2011, to May 31, 2012; and full generic competition, from June 1, 2012, to May 31, 2013.

### Table 3. Estimated Out-of-Pocket Spending for Brand-Name, Independent Generic, and Authorized Generic Atorvastatin

<table>
<thead>
<tr>
<th>Atorvastatin Prescription</th>
<th>Median (IQR), $</th>
<th>Estimated Monthly Out-of-Pocket Spendinga</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Market Exclusivity</td>
<td>Out-of-Pocket Spending per mg</td>
</tr>
<tr>
<td>Brand-name</td>
<td></td>
<td>0.02 (0.02-0.08)</td>
</tr>
<tr>
<td>Generic</td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Authorized generic</td>
<td></td>
<td>NA</td>
</tr>
</tbody>
</table>

**Abbreviations:** IQR, interquartile range; NA, not applicable.

*Based on per milligram spending multiplied by a 30-day supply of the most commonly dispensed dosage and strength in the Optum Clinformatics research database (20 mg).
to challenge potentially invalid patents.\textsuperscript{15} Our findings suggest that the FDA and Congress should consider whether the 180-day marketing exclusivity period is still useful and should be revised or eliminated.

Our study has limitations. We only examined trends in use and out-of-pocket spending with data from a single commercial claims database and for a single brand-name medication, albeit one of the best-selling drugs in the past 20 years.\textsuperscript{30} Our findings may not generalize to large public payors such as Medicaid or Medicare Part D or to patients who pay for prescriptions directly. Reports suggest that Pfizer aggressively and differentially negotiated with private payors and pharmacy benefit managers to win preferred formulary status and exclusive rights to mail order services for brand-name atorvastatin.\textsuperscript{6} The likely intent was to maintain market share as Lipitor’s market exclusivity was set to expire.\textsuperscript{2,5}

Another limitation inherent to segmented times series analyses is confounding by coexisting interventions. For example, other market forces such as Pfizer’s $4 copayment discount card may explain some of the trends of use that we observed. Beneficiaries may have chosen to use brand-name Lipitor if copayment discount cards made their out-of-pocket payments equal to those for generic atorvastatin.

Conclusions

Our analysis of changes in atorvastatin prescribing and costs found delays in generic uptake and high levels of out-of-pocket spending during the first 180 days after Lipitor lost market exclusivity. These delays slowed changes in drug use and decreases in patients’ out-of-pocket costs.

ARTICLE INFORMATION

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Conflict of Interest Disclosures: None reported.

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REFERENCES


In December 1996, 8 days before Christmas, the US Food and Drug Administration (FDA) approved Lipitor (atorvastatin; Pfizer) for the treatment of hyperlipidemia. Lipitor would become one of the most profitable prescription drugs in history, bringing in $130 billion in sales during its lifetime as a brand-name product and peaking at nearly $13 billion in sales in 2006 alone. Lipitor was far from the first statin in its class (simvastatin, pravastatin, and fluvastatin were already on the market), but 1996 was also the year that the FDA began allowing direct-to-consumer broadcast advertising. Lipitor was aggressively marketed based on its more potent lowering of cholesterol levels compared with other statins.

The story of Lipitor’s exit from the market—its loss of patent exclusivity—is as well-known as the story of its entry. The first generic version of atorvastatin was delayed owing to litigation and finally launched in November 2011. The generic received 6 months of market exclusivity, limiting the number of generic drugs that could compete until May 2012, when multiple other generics entered the market and the price dropped dramatically. Notably, Pfizer aggressively defended its sales territory during the 6 months between limited and full generic competition, providing incentives for insurers to keep Lipitor on their formularies and launching its own generic competitor. In a comprehensive analysis after the loss of Lipitor’s patent exclusivity, researchers with the National Bureau of Economic Research (NBER) used IMS Health sales data to document the change in out-of-pocket spending for patients when Lipitor lost patent protection and for the 6 months of limited generic competition that followed. It was only after June 2012—when multiple other generics entered the market—that the typical out-of-pocket cost for a month’s supply of generic atorvastatin decreased to $5.

In addition to confirming the findings of the earlier NBER analysis, the new study focuses on patient out-of-pocket costs. The delay in the introduction of low-cost generic atorvastatin affected not only overall drug spending, but also patient expenses. Using generic drugs is the primary means by which patients reduce their costs for prescription drugs. Thus, patients pay the price for any delays in the availability of generics. In the case of atorvastatin, it was not a backlog of generic applications at the FDA that limited access (and thus kept costs high), but the generic and brand-name manufacturers themselves, each fighting to extend the length of time they could sell their products with limited competition.

Although the focus on out-of-pocket costs in the study is important, 1 piece—simvastatin—is missing. In 2006, simvastatin (Zocor, marketed by Merck) lost its patent and a generic version became available. For many individuals—and most of the individuals in the cohort studied by Luo et al—of whom only 12.9% had documented coronary artery disease—simvastatin is appropriate for the treatment of hyperlipidemia. During the entire period studied by Luo et al, simvastatin was available as an inexpensive generic. Theoretically, the delay in access to generic atorvastatin should have affected only those individuals clearly in need of atorvastatin or a similar high-dose statin. The study does not provide information on the number of simvastatin users during the study period nor how many atorvastatin users received an 80-mg dose (and, thus, were not simvastatin candidates). However, the most common atorvastatin dose was 20 mg; thus, only a small percentage likely had a medical reason for using atorvastatin, not simvastatin.

Any analysis of the effect of generic atorvastatin entry on statin use should ideally account for the availability of simvastatin and other therapeutic substitutes. Most patients have no medical reason to take high-dose atorvastatin and can use other statins. For example, consider the limited effect of the delay in the availability of generic atorvastatin on statin use in the Department of Veterans Affairs (Figure). From December 2010 until June 2012, only minimal changes in the number of atorvastatin prescriptions occurred; instead, the use of pravastatin and rosvastatin increased slightly, with simvastatin decreasing in use but remaining by far the predominant statin. Individuals who required a more potent statin used rosvastatin, for which the Department of Veterans Affairs negotiated more

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**Invited Commentary**

**Prescription of Brand-Name Medications When Generic Alternatives Are Available—Patently Unfair**

Walid F. Gellad, MD, MPH; Chester B. Good, MD, MPH

In this issue of *JAMA Internal Medicine*, Luo et al analyze the change in use of atorvastatin and costs to patients after generic entry using data from a large national health insurer. From an examination of almost 2 million beneficiaries filling more than 13 million statin prescriptions, they show that loss of patent exclusivity for atorvastatin in November 2011 was associated with a modest reduction in monthly brand-name fills of 18.1%. In contrast, full generic competition by June 2012 was associated with a reduction of brand-name fills of 47.6%. More important, Luo et al document no meaningful reduction in out-of-pocket spending for patients when Lipitor lost patent protection and for the 6 months of limited generic competition that followed. It was only after June 2012—when multiple other generics entered the market—that the typical out-of-pocket cost for a month’s supply of generic atorvastatin decreased to $5.

In addition to confirming the findings of the earlier NBER analysis, the new study focuses on patient out-of-pocket costs. The delay in the introduction of low-cost generic atorvastatin affected not only overall drug spending, but also patient expenses. Using generic drugs is the primary means by which patients reduce their costs for prescription drugs. Thus, patients pay the price for any delays in the availability of generics. In the case of atorvastatin, it was not a backlog of generic applications at the FDA that limited access (and thus kept costs high), but the generic and brand-name manufacturers themselves, each fighting to extend the length of time they could sell their products with limited competition.

Although the focus on out-of-pocket costs in the study is important, 1 piece—simvastatin—is missing. In 2006, simvastatin (Zocor, marketed by Merck) lost its patent and a generic version became available. For many individuals—and most of the individuals in the cohort studied by Luo et al, of whom only 12.9% had documented coronary artery disease—simvastatin is appropriate for the treatment of hyperlipidemia. During the entire period studied by Luo et al, simvastatin was available as an inexpensive generic. Theoretically, the delay in access to generic atorvastatin should have affected only those individuals clearly in need of atorvastatin or a similar high-dose statin. The study does not provide information on the number of simvastatin users during the study period nor how many atorvastatin users received an 80-mg dose (and, thus, were not simvastatin candidates). However, the most common atorvastatin dose was 20 mg; thus, only a small percentage likely had a medical reason for using atorvastatin, not simvastatin.

Any analysis of the effect of generic atorvastatin entry on statin use should ideally account for the availability of simvastatin and other therapeutic substitutes. Most patients have no medical reason to take high-dose atorvastatin and can use other statins. For example, consider the limited effect of the delay in the availability of generic atorvastatin on statin use in the Department of Veterans Affairs (Figure). From December 2010 until June 2012, only minimal changes in the number of atorvastatin prescriptions occurred; instead, the use of pravastatin and rosvastatin increased slightly, with simvastatin decreasing in use but remaining by far the predominant statin. Individuals who required a more potent statin used rosvastatin, for which the Department of Veterans Affairs negotiated more

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