Current perspectives of U.S. Managed Care Organizations and Pharmacy Benefit Managers on the availability of 10 mg Lipitor OTC

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INTRODUCTION

According to the Centers for Disease Control and Prevention (CDC), people with high cholesterol have about twice the risk of heart disease as people with lower levels.[1] Heart disease is the leading cause of death in the United States.[1] Approximately 73.5 million adults (31.7%) in the United States have high low-density lipoprotein (LDL), or "bad," cholesterol.[2]

The U.S. introduction in 1991 of the statin, Zocor® (simvastatin), has been credited with increasing diagnosis rates of high LDL and with contributing to reducing the rates of heart attack and stroke attributed to high LDL in the United States.[3] Lipitor® (atorvastatin calcium) was introduced in the United States in 1996 with higher dosing than the highest labeled doses of Zocor, providing an option to patients who needed a more potent agent than Zocor.[3] Based on the retrospective analysis in the National Center for Health Statistics brief published in 2013, Lipitor contributed to an increased trend toward more patients being treated for elevated LDL.[4] Corresponding reductions in the rates of heart attacks and strokes during the time period were also observed in the CDC Chartbook published in 2011.[5] Crestor®, which launched in the United States in 2003, added to the statin armamentarium available for these same patients.[3]

In November 2011, 15 years after the launch of Lipitor, generic atorvastatin became available. This too has been attributed with making a positive impact on treatment rates, because it enabled access to this widely used statin at a lower cost for consumers. Currently, there are several generic statins available in the United States, although they all require a prescription. Several managed care organizations (MCOs) and pharmacy benefits managers (PBMs) offer generic statins, such as simvastatin and atorvastatin calcium, at copayments as low as $4, with some employers and health plans offering them free to members who switch from a branded agent such as Crestor.

Despite the availability of statins with proven track records in lowering LDL, including lower-cost generic versions, only one out of every three adults with high LDL cholesterol has the condition under control.[6] And while it is generally known that lowering cholesterol can reduce a person's risk of heart attack and death, fewer than half of the adults with high LDL cholesterol (48.1%) are receiving treatment to lower their levels.[2]

Recently, the American College of Cardiology (ACC) and the American Heart Association (AHA) issued revised Guidelines for the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults. The previous guidelines focused on achieving target cholesterol levels. The revised 2013 guidelines, instead, recommend an assessment of cardiovascular risk factors. The guidelines set thresholds for the 10-year risk of heart disease and stroke at 7.5% or higher, and recommend a tiered system of statins therapy to reduce risk.[7] The guidelines go on to say that non-statin therapies (e.g., niacin, fibrates, bile acid sequestrants, ezetimibe, etc.), whether used alone or in addition to statins, do not provide acceptable atherosclerotic cardiovascular disease (ASCVD) risk reduction benefits compared to their potential for adverse effects in the routine prevention of ASCVD.[7]

EXECUTIVE SUMMARY

Milliman conducted market research with pharmacy and therapeutics (P&T) committee members of U.S. MCOs and PBMs to gain their perspectives on the potential availability of 10 mg Lipitor over-the-counter (OTC). The market research reconfirmed some of the findings from a primary market research study published in the *Journal of Managed Care Pharmacy* (JMCP) in 2004, but also offers insights in previously unexamined areas. It should be noted that subsequent to the initiation of this research, Pfizer announced that it will not pursue approval for 10 mg Lipitor OTC.

Most of the payers interviewed believe that availability of an OTC statin could increase treatment rates of people with elevated LDL, which they perceive as a positive. Some national and regional MCOs suggested that the OTC product could be an opportunity for members who are known to be previously treated with a statin but who have not been filling their prescriptions (Rx) for a period of time (i.e., are non-adherent) to return to statin therapy. None of the payers indicated that they anticipate dropping coverage for atorvastatin or simvastatin in the higher strengths. However, in the scenario where Lipitor 10 mg is the only OTC statin available, a few indicated that they would remove prescription atorvastatin calcium 10 mg from coverage.

The market research suggests that PBMs will be the most resistant to 10 mg Lipitor OTC, which is due to significant potential negative revenue implications from reduced generic statin utilization as well as the potential impact on care, patient management, and quality programs they provide to employers and plans related to this therapeutic area.

It is incumbent upon the manufacturer of an OTC statin to ensure, to the extent possible, that consumers are well educated regarding the risks, benefits, and the target patient population intended for the OTC statin. That ensures that only the indicated patients seek treatment with the OTC version of the statin, and that patients under a physician's care are not diverted from their current Rx treatment regimen. This education should also ensure that consumers are made aware of how they can identify the need to seek medical attention when taking the OTC version.

This report was commissioned by Pfizer Inc. The findings reflect the market research conducted by the authors. Milliman does not endorse any product or organization. If this report is reproduced, we ask that it be reproduced in its entirety, as pieces taken out of context can be misleading. As with any market research study, it is not possible to capture all factors that may be significant. Because we present responses from a sample of the U.S. MCOs and PBMs, rather than a census of all such organizations in the United States, it may not be appropriate to extrapolate the findings.

METHODS

Initially, Milliman conducted an examination of literature to develop an understanding of U.S. payer perspective about how an OTC statin may impact LDL treatment rates and Rx statin coverage. As noted in the Discussion section of this paper, several issues with transferability of the findings were identified with the literature examined. Therefore, we decided that it was necessary to conduct primary market research with U.S. MCOs and PBMs to develop a more thorough understanding of the potential implications of an OTC statin in the current U.S. market environment—that is, following implementation of the Patient Protection and Affordable Care Act (ACA) and the generic atorvastatin calcium coming to the market. This report was developed to summarize that perspective as well as inform other related topics. For example, the research explored the possible impact on the formulary management of prescription statins by payers and whether they would promote awareness of the availability of an OTC statin to members even if they did not provide reimbursement for the OTC statin.

For this primary market research, we conducted interviews with 15 decision makers from six national MCOs, six regional MCOs, and three PBMs, which collectively cover over 140 million commercial and Medicare Part D (combined) lives. Although self-insured employers were not interviewed in this research, the perspective of those employers was researched by asking the PBM respondents to elaborate on any differences they have observed between the perspective of their self-insured employer clients and that of their health plans clients. We investigated their perspectives on the potential introduction of OTC statins, with particular interest in low-dose (10 mg) Lipitor.

We conducted telephone interviews with the 15 participants during April 2015. The interviews were each 60 minutes in duration. Participants were tenured, active voting P&T committee members whose current roles were chief medical/pharmacy officer or medical/pharmacy director in their respective organizations. We allowed only one participant per payer organization and we did not interview any retired or former employees. All participants had experience as practicing clinicians, either pharmacy or medical, at some point in their career. The market research was conducted as a double-blind study where participants were not made aware of the sponsor of the study and the sponsor of the study was not made aware of the identity of the participants or their employers. Participants were made aware during recruiting for the study that the purpose of the interviews was for the development of a white paper on this topic and that their names and their organizations' names would not be directly attached to any of their responses in the paper.

Research participants were not required to perform any analysis or read any information about the topic in advance of the interviews. During the course of the interviews they viewed information via WebEx to allow them to provide feedback on two items: the 2013 ACC/AHA Guidelines for the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults and a potential future 10 mg Lipitor OTC and Lipitor Rx (formulary prescription) scenario. We reminded participants that the information discussed is confidential and that no OTC statin approved by the U.S. Food and Drug Administration (FDA) is currently available in the U.S. market.

Milliman leveraged observations from previous primary market research studies we have conducted on the topics of cardiovascular disease, Rx statins, and OTC pharmaceuticals in the creation of the research instrument used for this primary market research. All interviews followed a predefined set of questions that populated a discussion guide used by the moderator conducting the interviews. An outline of the topics covered in each interview is shown in Figure 1.

Figure 1: Topics Covered in Interviews

Current Formulary Status of Rx Statins. This section established how each participant's organization currently covers branded and generic statins on the formulary, including the tier status and any management edits for each product for their dominant commercial benefit design

and for the Medicare Prescription Drug (Part D) benefit (for those participants with both lines of business).

Benefits of Statins for Primary and Secondary Prevention. The participants were asked to review the 2013 revision to the ACC/AHA Cholesterol Guidelines. Then, we asked for the participant's view on the value of making statins available on the formulary, in general, and their view of the benefit of statins for Primary or Secondary Prevention.

OTC Statin Impact on Member Willingness to Seek Treatment. Participants were asked to suggest the impact an OTC statin would have on member willingness to seek treatment for elevated LDL.

Perceptions of the Introduction of 10 mg Lipitor OTC. Participants were introduced to a scenario in which 10 mg Lipitor OTC would be available. The scenario provided information such as how the 10 mg dose aligns to the ACC/AHA Cholesterol Guidelines and who the appropriate patients would be given the proposed indication. Participants were asked to provide their perspective on the positive and negative implications related to this scenario.

Suggested Rx Statin Formulary Coverage and Restrictions Post-10 mg Lipitor OTC Introduction. Participants were asked how this Lipitor 10 mg OTC scenario would impact their formulary approach to the Rx statins.

Anticipated Impact on Statin Volume and Anticipated Source of 10 mg Lipitor OTC Utilization. Participants were asked how this 10 mg Lipitor OTC scenario would impact statin volume. This was followed by a discussion of the intended population for 10 mg Lipitor OTC and participants were asked who they believed the appropriate patients would be.

Value Payers Would Derive from the Introduction of 10 mg Lipitor OTC. Participants were asked questions regarding the value that could be derived by their respective organization and members from the availability of 10 mg Lipitor OTC.

The intention of this study was not to provide a quantitative analysis of the market, but rather to develop insights in a qualitative manner regarding the prevailing perspectives in the market. Therefore, the findings from the 15 interviews were synthesized to assess the observations broadly, rather than on an organization-by-organization basis. The next section of this report provides key observations from the questions posed to the participants in the market research study. Where appropriate, tables are used to illustrate the findings.

MARKET RESEARCH FINDINGS

Current formulary status of Rx statins

All participants make generic statins available on their commercial and Part D formularies at tier 1, except one payer that has simvastatin on tier 1 and all other generics on tier 2. This MCO's dominant employer-funded benefit design is four tiers with generics on tiers 1 and 2 and brands on tiers 3 and 4. Crestor is available on the preferred brand tier for 97% of the participants' commercial enrollment and 98% of the participants' Part D enrollment. Where Crestor is not preferred, other branded statins were also not preferred.

Figure 2: Current Formulary Status of Rx Statins of Payers Interviewed

Formulary Restrictions	Branded Rx Statin Formulary Coverage	Formulary Status Response by Payer Type	Commercial Formulary [b] % of Lives[d]	Medicare Formulary [c] % of Lives[d]
None	Crestor, NP [a]		<1%	<1%
	Crestor, P; All Others[e], NP		51%	76%
	Crestor, P [f,g]			
	Crestor, P; Lipitor, NC; All Others[e], NP			
SE or PA	Crestor, P; All Others[e], NP		46%	22%
	All Brands, NP		3%	2%
	Crestor & Livalo, NP; All Others[e], NC			

[a] All 15 plans indicated that generic statins are covered on Tier 1 with no restrictions, except one regional MCO with differentiated generic coverage in commercial their formulary: simvastatin is T1, other generics T2, Brands are T3 & 4
[b] Commercial formulary shown is the fully insured pharmacy benefit offered by the payer that is most often purchased by employers. For PBMs this is defined as the non-ASO lives of their health plan clients
[c] Responses for Medicare were general answers for the channel
[d] % of lives summarizes the distribution of responses received. Sums to 100% for each payer channel. Figures are rounded to the nearest %. Composite % by category is used to ensure confidentiality of each respondent is maintained.
[e] "All Others" refers to all other statin brands
[f] Only coverage for Crestor was clearly identified. Other brands such as Lipitor and Livalo were not specifically mentioned and therefore could be either Not Preferred or Not Covered
[g] One of the 15 plans (regional MCO) has no Medicare formulary.

* Each icon represents one response per interview, for a total of 15

SE = Step Edit; PA = Prior Authorization; P = Preferred; NP = Not Preferred; NC = Not Covered

Icon Legend: Regional Managed Care Organization; National Managed Care Organization; Pharmacy Benefits Manager

Although Crestor is a preferred agent for nearly all enrollment represented in the research, a step-edit (SE) or prior authorization (PA) is present for 46% of employer-funded lives and 22% of Part D lives. And, for the 3% and 2% of employer-funded and Part D lives, respectively, where Crestor is not preferred, there is also an SE or PA in place.

The SE and PA criteria ranged from a single step through generic simvastatin or atorvastatin calcium to one formulary with "or" criteria, where the member would need to have a documented contraindication, intolerance, allergy, or failure to a one-month trial of each of the preferred generics before having access to Crestor. The most common criteria was a required failure on two generics at the 40 mg or higher dose.

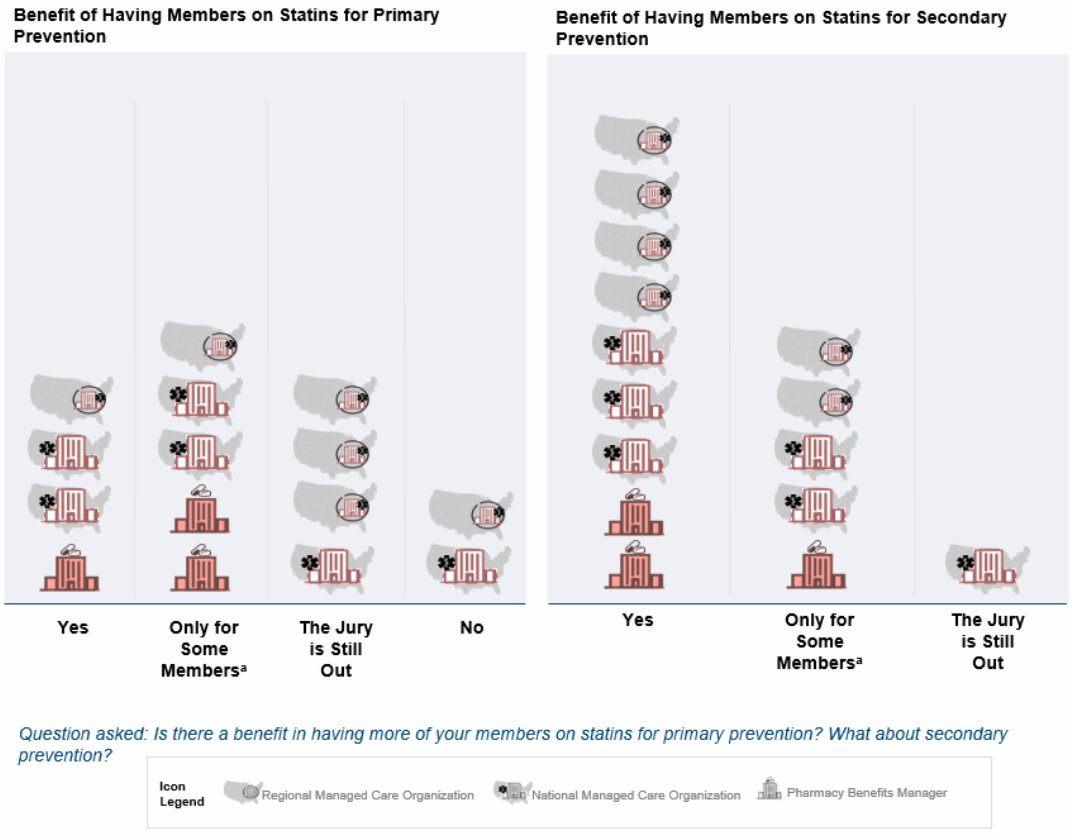
Failure was described by these payers as either documentation by the prescriber that the patient did not respond adequately to the therapy or a lab test showing lack of improvement on the patient's LDL score.

Benefit of having members on statins for primary and secondary prevention

Participants were shown a summary of the 2013 ACC/AHA Guidelines and all were familiar with them and understood them, with some participants indicating that they had modified policies because of the update.

While a majority of the participants agreed that there is benefit in their members being on a statin for Secondary Prevention, fewer agreed that this is also true for Primary Prevention. A little more than half of those who believe there is benefit for Primary Prevention offered the caveat that there is only benefit in Primary Prevention if the member is also co-morbid with diabetes, has significant cardiovascular risk factors, is known to be moderate to moderately high risk, or all of these. Nearly a quarter of the participants questioned whether data supports statin treatment for Primary Prevention, with some citing the 2013 ACC/AHA Guidelines as the reason for their skepticism.

Figure 3: Benefits of Having Members on Statins for Primary and for Secondary Prevention

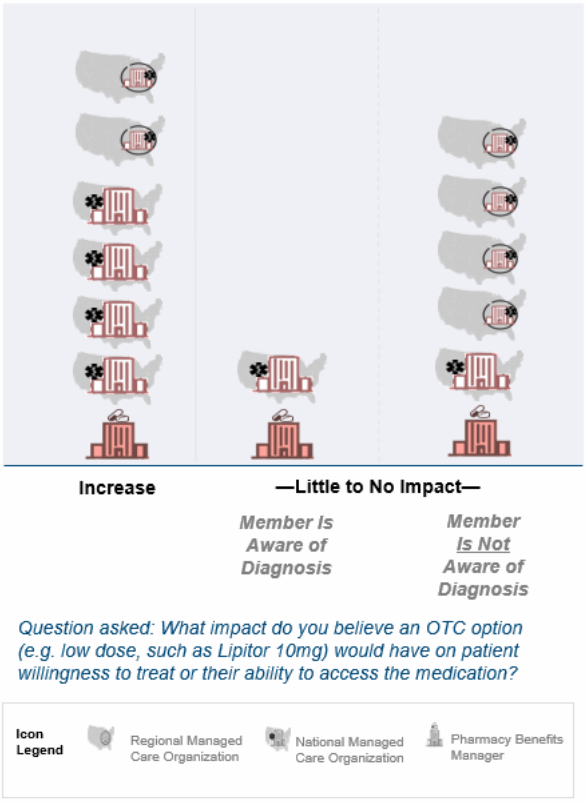


Impact of OTC statin availability on treatment rates for elevated LDL

Most of the payers believe that the availability of an OTC statin could increase treatment rates for high LDL, which they perceive as a positive. In addition, most suggested, or agreed when asked, that the greatest barrier to treatment is that patients either avoid being seen by a physician for treatment or they have issues that get in the way of going to their physician. A little less than a quarter of the participants

suggested that members with high-deductible health plans and members taking multiple prescriptions (for multiple co-morbidities) would be some of the likely purchasers of the OTC statin.

Figure 4: OTC Statin Impact on Member Willingness to Seek Treatment



When asked how large the currently untreated (with statin) high LDL population is, nearly all participants had difficulty quantifying this population, although all indicated they believe it is a significant number. Further to this point, they did not have suggestions for how to quantify the subpopulation of moderate to moderately high-risk patients. It should be noted here that this subpopulation is different from the population discussed in the 2004 study published in JMCP, which focused on low- to moderate-risk patients.

Positives and negatives of 10 mg Lipitor OTC availability

Participants were shown a specific 10 mg Lipitor OTC scenario (Figure 5), which included a proposed indication, intended treatment population, and where it fits within the 2013 ACC/AHA Guidelines.

Figure 5: Potential Lipitor OTC Scenario

Lipitor OTC

- Available in 10 mg dose only
- Indicated to lower cholesterol (for primary prevention) for patients with moderate to moderately high risk of cardiovascular disease
- Labeled to exclude patients currently using statins, unless they consult their physician first
- Falls within the 2013 ACC/AHA Guideline recommendations for initiation of statin treatment in moderate to moderately high risk patients

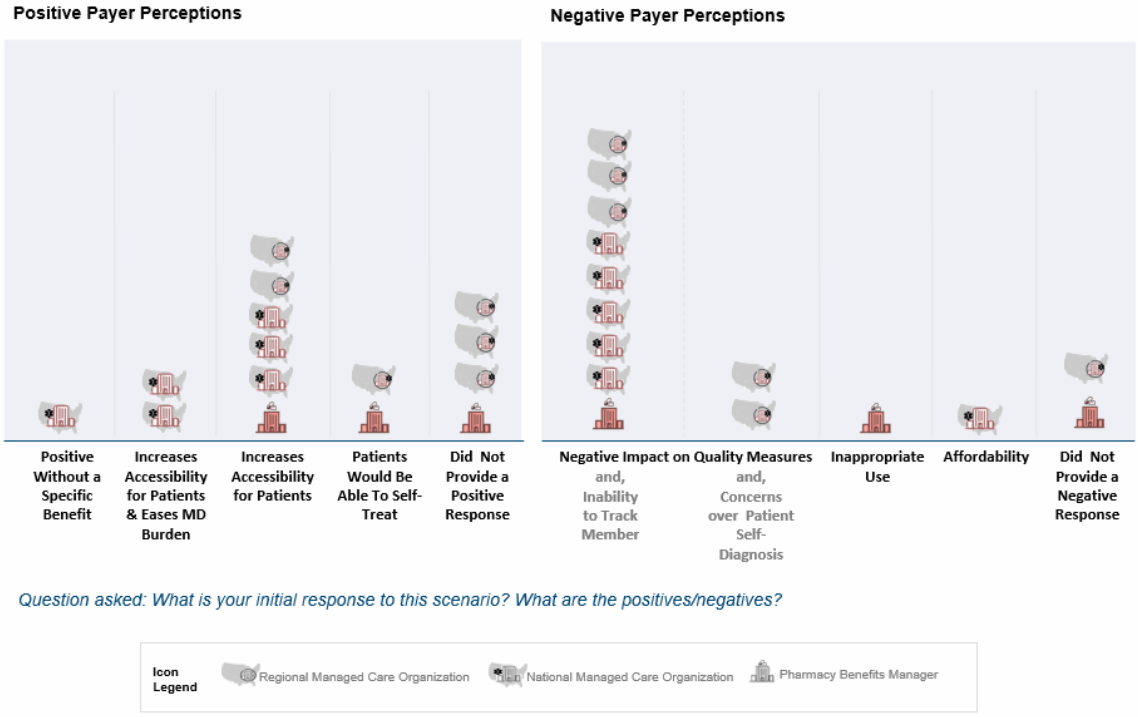
Lipitor Rx will be available in 10 mg for some indications and the 20 mg,40 mg,80 mg strengths will remain available for other indications for the currently labeled patient populations

Payer participants were asked what they thought the most important benefit from the availability of 10 mg Lipitor OTC would be. The most common positive response was that it would increase accessibility. Several of these payers were quick to point out that accessibility and access are not synonymous when speaking of OTCs. They clarified that accessibility means increased potential for members to acquire the medication because the burden and/or cost of seeing a physician are removed; access may still be an issue for some members if the OTC is priced similarly to some other OTCs that were recently introduced.

Before answering this question, many participants went through a mental exercise of balancing the risks of known consumer behavior with OTCs (such as acetaminophen) and the clinical benefit of having an OTC statin available, given how important it is to treat elevated LDL. Most struggled to identify specific benefits for the moderate- to moderately-high risk population, with several questioning how members would know they are moderate- to moderately-high risk without prior physician consultation.

Participants were also asked to provide what they thought were the most important negatives. The negative expressed by two-thirds of the payers interviewed is the potential loss of statin Rx data for tracking quality measures for members currently taking statins, who then decide to convert to the OTC. For plans with Medicare Advantage Prescription Drug Contracting (MAPD) beneficiaries, in addition to tracking for the Medicare Five-Star Quality Rating System, a significant clinical concern cited was losing the ability to track members. The clinical concern was cited for commercial beneficiaries as well. A few expressed a concern over either affordability, issues with member self-diagnosis, or inappropriate use.

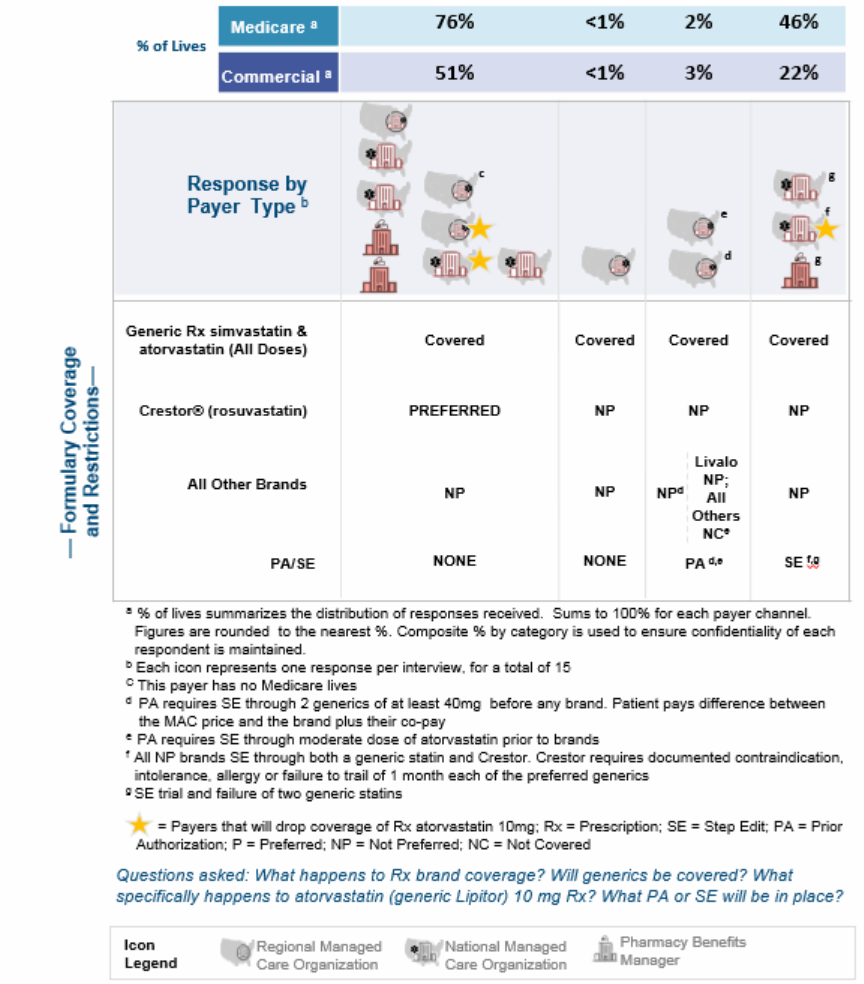
Figure 6: Positive and Negative Payer Perceptions of the Introduction of 10 mg Lipitor OTC



Impact of 10 mg Lipitor OTC availability on Rx statin formulary

Most payers interviewed said that the availability of 10 mg Lipitor OTC would not change anything from a formulary perspective for their employer-sponsored or Part D pharmacy benefit. Three of the 15 payers (representing 25% of employer-sponsored lives and 7% of Part D lives in this research) said they would remove atorvastatin calcium 10 mg from the formulary, which is the same strategy employed with other therapeutic areas where an OTC version was introduced.

Figure 7: Respondent-Suggested Rx Statin Formulary Coverage and Restrictions Following Introduction of 10 mg Lipitor OTC



Although wavering by some participants was observed regarding whether to maintain 10 mg atorvastatin calcium on the formulary, the following were some of the reasons for not removing coverage:

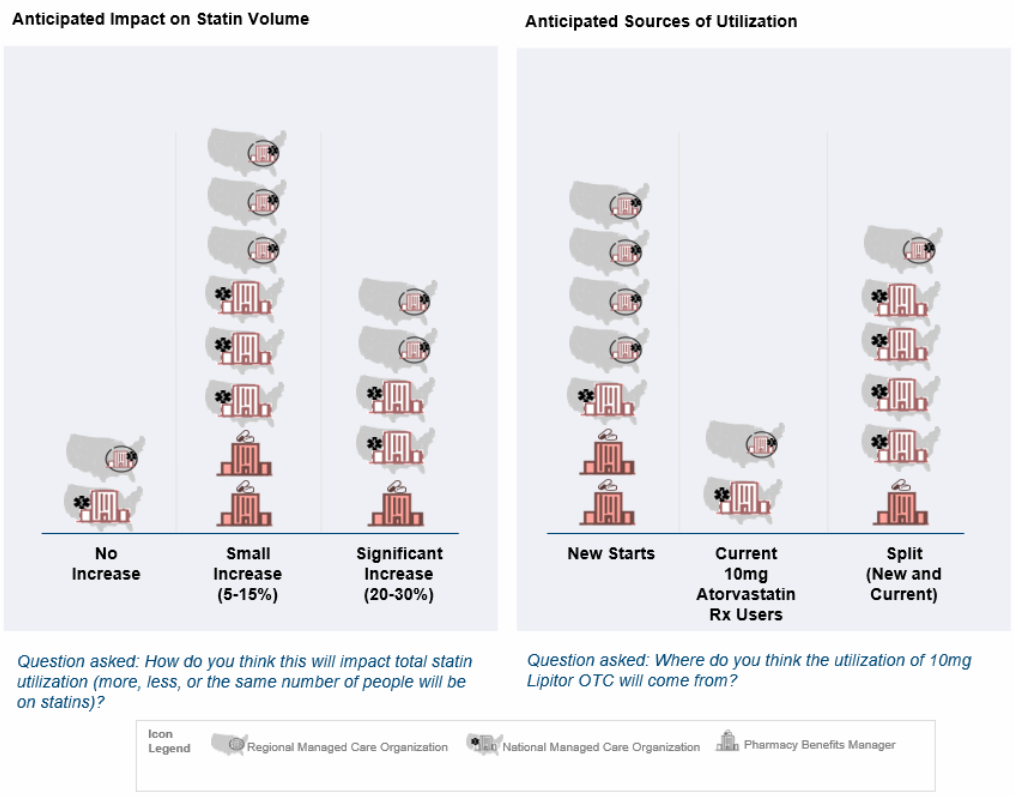
- Utilization will move to higher Rx strengths otherwise
- 10 mg Lipitor OTC is expected to be expensive like Nexium OTC, which is viewed as an affordability issue for their members and could cause them to stop taking their statins
- Quality measures would be negatively impacted
- It is too sensitive (high utilization) of a category to drop atorvastatin calcium or simvastatin from Part D plans

A few participants considered adding failure on 10 mg Lipitor OTC to their failure on a generic SE, but reversed themselves, citing lack of visibility to the member trial of OTC as the reason.

Impact on statin volume and source of utilization for 10 mg Lipitor OTC

Payers were asked where they believe 10 mg Lipitor OTC use could come from and what impact the introduction would have on overall statin volume. Most suggested they expect it to come from new starts, which would result in a modest increase in overall statin utilization. Half these payers suggested these new starts would be the same people who currently purchase Omega 3s OTC to manage their high LDL. The reason most often offered for the belief that there would be minimal uptake of the OTC was the payers' assumption that the cost of the OTC would be similar in magnitude to that of the latest OTC introductions in other therapeutic areas. In addition, participants pointed out that generic statins are "very cheap at $4" or are free for a majority of covered members.

Figure 8: Anticipated Impact of 10 mg Lipitor OTC on Statin Volume and Sources of Utilization

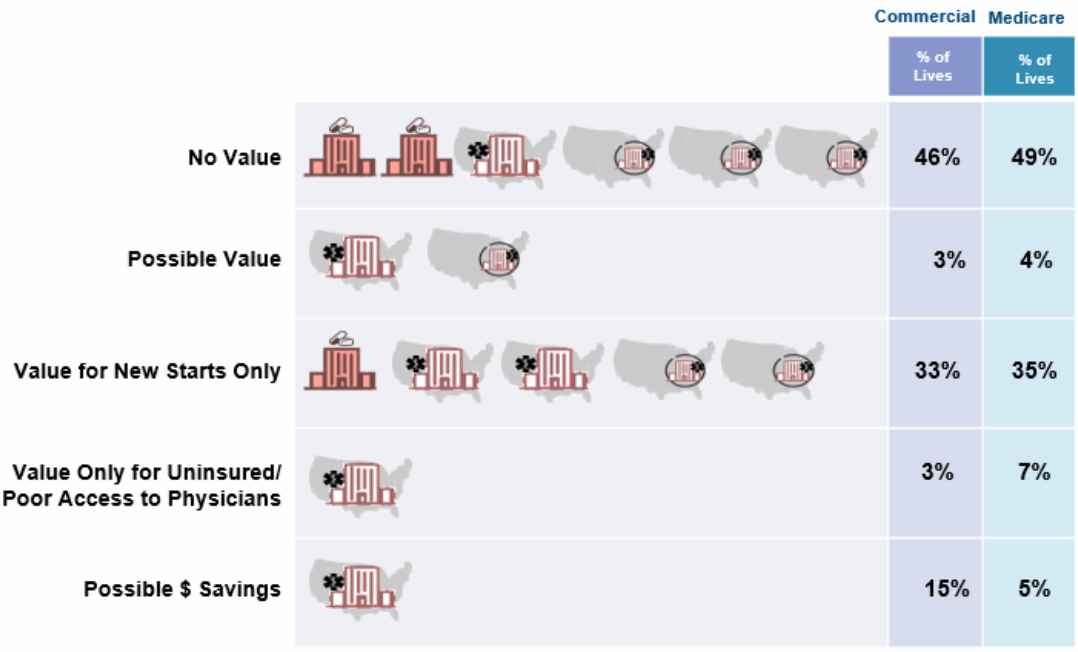


MCO/PBM support for 10 mg Lipitor OTC availability

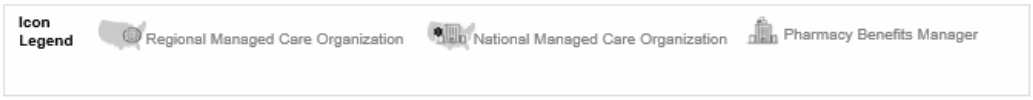
Payers expressed the need to balance their concerns (patients who need to be under the care of a physician, loss of tracking members, etc.) against the need to treat those who are currently untreated, when determining whether or not they support the OTC statin concept. Four MCOs and two PBMs settled on the premise that there is no value to them in supporting the introduction of the OTC and that they would not actively engage in support for it with their members. Five, including one PBM, said it is possible for them to support the concept, but only for new starts. The remaining four were split between two that agreed there is possible value, while still not wanting to engage in active support, and two that agreed that, if there were cost savings, they could support it, or it could only be supported for those without insurance (which falls outside of their membership).

The two PBMs who said there is no value to them in supporting the introduction also indicated that they would not take any action against it either; while the third PBM participant (who said it is possible to support the concept) also acknowledged that there are negative aspects to this.

Figure 9: Value Payers Would Derive From the Introduction of 10 mg Lipitor OTC



Question asked: What value, if any, do you believe your plan would derive from actively promoting this particular OTC to employers/members?



DISCUSSION

As noted in the Methods section, Milliman conducted a literature search going back more than a decade to establish a historical perspective on OTC statins as well as a baseline for understanding payer attitudes toward OTC introductions in general and statins in particular. Although the literature provided some evidence regarding payer perspectives and relevant market dynamics that could be used to infer how Rx statins would be impacted if an OTC statin were to be introduced, a number of limitations were noted and are described in this section.

OTC medications require FDA approval but they do not require a prescription or physician consultation. Although there is currently no OTC statin available in the United States, viewpoints on the pros and cons of OTC statins have been observed in press releases, media stories, and published journal articles dating back to the Pravachol® OTC switch attempt by Bristol-Myers Squibb (BMS) in 2000, which was rejected by the FDA. One prevailing perspective is that the introduction of an OTC statin could lead to greater awareness and higher treatment rates of people with elevated LDL.[8] Proponents of this perspective suggest that statin-adherent members would receive the clinical benefit of lower risk for stroke and heart attack, and at the same time payers would receive real-time cost savings from not paying for Rx statins, as well as potential long-term cost savings from cardiovascular event reduction.

A somewhat different perspective is skeptical that the availability of an OTC statin will improve clinical outcomes. This perspective doubts that a person with elevated LDL who is not under a physician's care or who are not taking a statin would be aware of their condition or understand enough to enable self-diagnosis and safely use an OTC statin.[9] This line of reasoning seems to originate from anecdotal evidence of consumer behavior with OTCs such as nonsteroidal anti-inflammatory drugs (NSAIDs) and other widely used OTC medications, as well as knowledge of the unsuccessful OTC statin conversions by BMS for Pravachol in 2000, and by Merck for Mevacor® in 2000, 2005, and 2007.

We begin our discussion of the literature with an article published in the American Journal of Cardiology in 2004 on the topic of possible U.S. consumer behavior with OTC statins.[10] The Consumer Use Study of OTC Mevacor (CUSTOM) evaluated the ability of subjects to self-manage high levels of LDL cholesterol by using a multifaceted cholesterol self-management program, the Mevacor Over-the-Counter Self-Management System (MOTC-SMS). The study was conducted over 26 weeks as a multicenter all-comers observational study in a naturalistic storefront setting using MOTC-SMS to guide subjects' behavior. Of 3,316 subjects evaluating the product (evaluators), 1,061 took a dose of at least a 20 mg tablet of Mevacor OTC (users). Most users in the CUSTOM study demonstrated ongoing product use behavior in the areas such as treatment to goal, compliance/persistence, and changes in health status in a manner that was deemed acceptable relative to the criteria and directives on the Mevacor OTC label. Only 23 (2%) of the users exhibited behavior that produced the potential for safety concerns.

The results of this study showed that after 26 weeks, 62% of the 878 patients who completed the study achieved the treatment goal of LDL cholesterol below 130 mg/dL. The authors concluded that the MOTC-SMS system was effective in guiding consumers to make appropriate preliminary and ongoing self-treatment decisions, which included consultation with healthcare professionals. CUSTOM was part of the New Drug Application (NDA) package submitted to the FDA by Johnson & Johnson/Merck in 2005. The FDA Nonprescription Drugs and Endocrinologic & Metabolic Drugs Advisory Committees, however, did not agree that the CUSTOM study demonstrated that Mevacor 20 mg OTC could be used safely and effectively as an OTC agent and rejected the NDA in a 20-to-3 vote.[11]

We also examined literature that discussed real-world patient behavior with OTC statins where financial implications were also observed. Simvastatin 10 mg has been available for purchase without a prescription since May 2004 in the United Kingdom (UK).[12] A 2012 article was published on this topic by Health Services Research in the UK. It should be noted that in the UK the term "behind-the-counter" (BTC) is used when referring to a "pharmacy only" drug. This differs slightly from OTC in the United States because, although a consumer does not need a prescription, he or she must consult with the pharmacist in order to make the purchase. This retrospective study examined secondary data on simvastatin utilization, prices, and expenditures for the 10-year period from 1997 to 2007 in the UK (and four other countries) in order to assess

the period of time before the introduction of BTC simvastatin relative to the period of time after. The authors concluded that the introduction of BTC simvastatin in the UK led to a significant increase in utilization of simvastatin and a significant decline in insurer expenditures for simvastatin purchases. Extending these results directly to the United States requires further analysis, which is due to differences in the healthcare markets between the United States and the UK, most noteworthy being the single payer system of the UK versus the dominant private payer system of the United States. In addition, the introduction of simvastatin in the UK was BTC rather than OTC.

We also evaluated the findings of a U.S. payer market research study that was conducted in 2003 and published in JMCP in 2004.[13] This study was conducted with U.S. payers specifically on the topic of OTC statins. The authors concluded that the payers interviewed considered the introduction of an OTC statin a low risk and a beneficial addition to drug therapy and that payer policies would continue to support access to prescription statins with no change in policy following introduction of an OTC option. Most study participants believed that increased awareness would result in an initial increase in plan costs, but long-term savings would accrue through improved care and availability of lower-cost OTC options for low- to moderate-risk patients. The key concern expressed by the payers in the study was how to help patients gain enough knowledge and comfort to manage their own cholesterol therapy safely and successfully. Four important market factors had yet to come to fruition when this study was completed which makes the conclusions of this study less relevant to the current market. This study was conducted in 2003, which is the same year Crestor launched and there was very little real-world experience with that statin; and it was also conducted three years before generic simvastatin was introduced in 2006. Additionally, the Patient Protection and Affordable Care Act (ACA) was not implemented until early 2010. The ACA has had a dramatic impact on health plan economics. Lastly, the dominant market leader, Lipitor, did not lose patent exclusivity until late 2011.

Finally, we considered whether recent OTC switches in other therapeutic areas may provide evidence points, following implementation of the ACA, to understand likely consumer behavior and financial implications of the availability of OTC statins in the current market environment. In the United States, non-sedating antihistamines, proton pump inhibitors (PPIs), and, most recently, a 2015 OTC introduction of a corticosteroid nasal spray for allergies have made the transition from Rx to OTC. Transferability of observations from these OTCs to statins is an issue. These OTCs are indicated for symptom control of somewhat benign conditions such as allergies and heartburn; whereas statins treat the cause of the asymptomatic condition of elevated LDL with a treatment goal of preventing serious, high-cost cardiovascular events.

The primary market research Milliman conducted with payers for this paper builds on the baseline observations provided in the literature discussed above and also extends on the findings from the 2004 JMCP study. Most notable of these findings is that payers would maintain coverage for the Rx statins currently covered, with an exception in some cases of the dose that would be available OTC.

Final considerations for pharmaceutical manufacturers

After the primary market research with payers was completed, but prior to the finalization of this white paper, Pfizer terminated its program to pursue NDA submission for 10 mg Lipitor OTC. According to an August 3, 2015, article in *The Tan Sheet*, a 1,200-patient actual use trial to simulate the use of 10 mg Lipitor OTC, which concluded in December 2014, did not meet its primary objective of demonstrating patient compliance with the direction to check their LDL level and, after checking, to take appropriate action based on the results. A Pfizer source quoted in the article indicated that the 10 mg Lipitor OTC program was terminated based on a dialogue with the FDA about the program and results of the actual use trial.[14]

The history of unsuccessful OTC statin conversion attempts by BMS, Merck, and now Pfizer seems to validate a concern expressed by some payers in the market research: the unknown ability of consumers to safely and effectively use an OTC statin. The obstacle that a manufacturer must solve in order to achieve a successful OTC statin conversion continues to be patient education. Until then, the potential clinical benefits for compliant OTC statin consumers and the possible long-term financial benefit accruing to payers that is due to event reduction among compliant OTC statin users will remain elusive.

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Milliman is among the world's largest independent actuarial and consulting firms. With more than 3,000 employees and revenues of USD 838 million in 2014, the firm serves the full spectrum of business, governmental, and financial organizations. Milliman was founded in 1947 and today has offices in principal cities worldwide, covering markets in North America, Latin America, Europe, Asia and the Pacific, the Middle East, and Africa.

Primary practice areas

- Employee benefits, investment, and compensation consulting services
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Milliman is owned and managed by approximately 400 principals, who have been elected in recognition of their technical, professional, and business achievements.

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Milliman is the leading provider of actuarial and related products and services to insurance markets worldwide.

ENDNOTES

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