
Patent Expiry Impact Predictor

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Patent expiries in the US statin market: Generics to slash market size by 80 per cent over the next ten years

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OVERVIEW OF THE US STATIN MARKET

Sales of branded statin monotherapies in the US at the end of 2005 reached US\$15.1bn, or 78 per cent of the entire US antidyslipidaemics market, up 2.3 per cent on 2004 sales (source: MIDAS sales; IMS Health, March 2006). Key drivers of this commercial success included aggressive, multi-channel marketing by big pharma, in the shape of Pfizer and Merck, and an overwhelming body of data derived from clinical trials that shows aggressive reductions of elevated cholesterol, particularly low-density lipoprotein-cholesterol (LDL-C), with statins reduces the risk of cardiovascular outcomes.^{1–4} At the product level, it was Pfizer's Lipitor (atorvastatin) that dominated the market with sales of US\$8.1bn, or 54 per cent market share, followed by Merck & Co.'s Zocor (simvastatin) and four other branded products, as illustrated in Table 1.

Of the six branded statins that are currently marketed in the US, only one was exposed to generic competition at the beginning of 2006; Merck & Co.'s Mevacor (lovastatin). Mevacor's US patent — US04231938 — expired in June 2001. While sales of Mevacor fell as a result of generic competition, sales of all other branded statins have been relatively unaffected by the availability of generic lovastatin. The key element of this lack of generic erosion centres on the perception that lovastatin is not as effective as other statins in reducing LDL-C and cardiovascular events, such as heart attacks and strokes.

IMPACT OF ZOCOR AND PRAVACHOL LOSING PATENT PROTECTION IN THE US

Since the beginning of 2006, Merck & Co.'s Zocor (simvastatin) and Bristol Myers Squibb's Pravachol (pravastatin) have lost patent protection, with the next high-profile loss expected in 2011 when Pfizer's Lipitor (atorvastatin) succumbs to generic competition (Table 2). As Pravachol only accounts for around 10 per cent of the branded statin market, generic pravastatin is not expected to have a huge impact on branded statin sales. As for lovastatin, reasons for this include physician preference for more potent statins supported by outcome data.

In contrast, many believe that simvastatin is as potent and effective as atorvastatin, a claim that Pfizer has rigorously disputed in the weeks running up to Zocor's patent expiry, and as such it is the loss of patent protection for Zocor that is expected to have a significant impact on the branded statin monotherapy market in the US. It has been estimated that if Medicare beneficiaries were prescribed low-cost generic statins instead of higher-priced brands, around US\$2,300 and US\$5,000 per year could be saved per patient, with some estimating that in excess of US\$8bn could be saved in 2007 alone.⁵ On this basis, many Pharmacy Benefit Managers (PBMs) and Managed Care Organizations (MCOs) in the US have been switching patients from other branded statins to

Table 1: The US statin monotherapy* market, 2005

Brand	Generics	Marketing company	SUs 2005 (m)	Growth 2004–05 (%)	Sales 2005 (US\$m)	Growth 2004–05 (%)
Lipitor	Atorvastatin	Pfizer	3,200	2.7	8,064	8.5
Zocor	Simvastatin	Merck & Co.	1,566	(7.7)	4,206	(4.7)
Pravachol	Pravastatin	BMS	500	(19.9)	1,655	(13.9)
Crestor	Rosuvastatin	AstraZeneca	345	23.8	797	36.3
Lescol	Fluvastatin	Novartis	184	(12.6)	336	(8.3)
Mevacor	Lovastatin	Merck & Co.	3	39.3	8	(36.4)
Total			5,798	(2.3)	15,066	2.3

Does not include sales of combination therapies (eg Vytorin, Caduet)

BMS – Bristol Myers Squibb

Source: IMS MIDAS sales data, IMS Health, March 2006

Table 2: Patent position for each of the statins in the US

Brand	Generic	Marketing company	Expiry date	US patent number
Mevacor	Lovastatin	Merck & Co.	Jun 2001	US04231938
Pravachol	Pravastatin	BMS	Apr 2006	US04346227
Zocor	Simvastatin	Merck & Co.	Jun 2006	US04444784
Lipitor	Atorvastatin	Pfizer	Jun 2011	US05273995
Lescol	Fluvastatin	Novartis	Apr 2012	US05354772
Crestor	Rosuvastatin	AstraZeneca	Jun 2012	US05260440

Source: Dolphin, accessed July 2006, ©Thomson Scientific; FDA Orange Book, accessed July 2006; MedTRACK, July 2006, ©Datamonitor plc

Zocor since 2005 in preparation for Zocor's patent expiry.

SWITCHING SCENARIOS FOR ZOCOR; GENERIC IMPACT IS LIKELY TO BE HUGE

Two key factors will have an impact on future Zocor sales — the level of switching from Zocor to generic simvastatin, and the price difference offered by the generic alternatives. Given the following set of assumptions, Datamonitor has estimated sales forecasts for Zocor:

- US sales of Zocor were US\$4.2bn in 2005 (Midas Sales Data, IMS Health, March 2006);
- three generics will be launched within the first six months of patent expiry — Teva's and Ranbaxy's first-to-file, and Dr Reddy's authorised generics;
- around eight additional generics will be launched after the expiration of the

180-day exclusivity period, with a further 10–15 being launched by the end of the forecast period.

Despite Merck & Co.'s attempts to limit the impact of generics on Zocor revenues by inking a deal with US health insurer United Health Group whereby branded Zocor would be less expensive than the generic versions, it is still expected that other healthcare providers will continue to push for maximum switching to generic simvastatin. In line with preliminary switching data,⁷ Datamonitor expects that in the first six months following patent expiry, a high (75–80 per cent) level of switching from Zocor to generic simvastatin will take place, the impact of which is illustrated in Figure 1 along with low (20 per cent) and medium (50 per cent) switching scenarios.

While there are a number of measures being employed in the US to encourage switching from branded drugs to cheaper

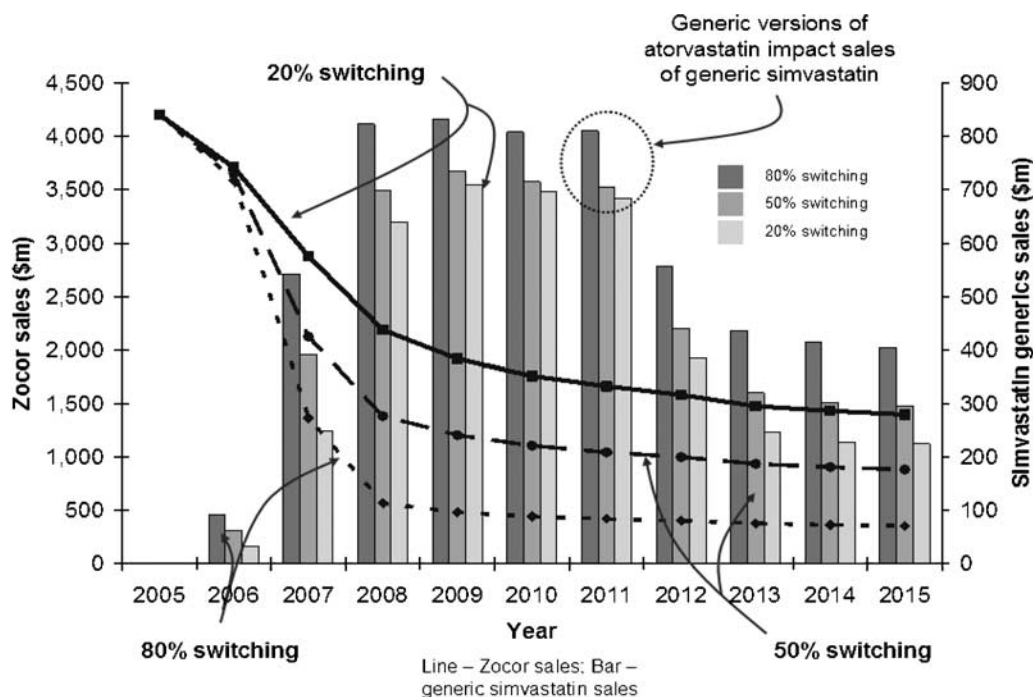


Figure 1: Likely scenarios for switching from Zocor to generic simvastatin, and the effect of generic atorvastatin from 2011 on generic simvastatin sales Source: Datamonitor

generic alternatives, one of the key measures is the encouragement of step therapy — the use of cheaper therapy initially followed by more expensive therapy later, should the cheaper therapy be ineffective — and the cumbersome prior authorisation process employed by many PBMs in the US. That said, assuming a 35 per cent price difference between Zocor and generics in the first six months, falling to 75 per cent thereafter, sales of generics are likely to grow rapidly at the expense of Zocor as extensive switching takes place. As such, sales of Zocor are likely to reach of US\$3.6bn in 2006, US\$565m in 2008 and US\$440m in 2010.

IMPACT OF GENERIC SIMVASTATIN ON SALES OF LIPITOR; CAN THE GIANT SURVIVE?

Therapeutic substitution between Lipitor and generic simvastatin is expected, the degree of

which will depend on how many healthcare providers consider atorvastatin and simvastatin therapeutically equivalent. Indeed, the first signs of switching have been recorded in Pfizer’s first-quarter 2006 results, where Lipitor experienced nearly flat growth of 3 per cent in the US compared to the same period of 2005.⁶ Additionally, recent new prescription data⁷ show that new prescriptions for Lipitor fell by 10 per cent between June 30 and July 7, 2006, with generic simvastatin prescriptions growing by 80 per cent in the same period.⁸

Ultimately, Datamonitor believes that the most likely level of initial switching will be around 30 per cent of current Lipitor patients. Pfizer has not, so far, announced plans to reduce the price of Lipitor to retain patients. Thus, Datamonitor does not expect Pfizer to reduce the price of Lipitor to combat competition from generic simvastatin in the US. Moreover, prescription data for Lipitor during the week ending July 14, 2006 suggest

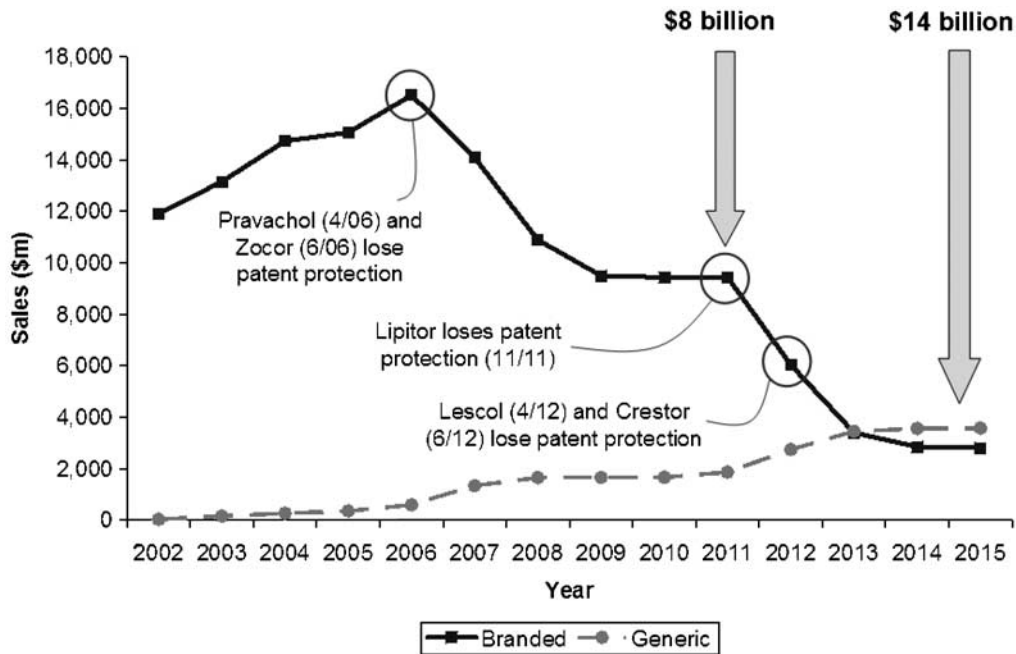


Figure 2: Between 2006 and 2011, the value of the branded US statin monotherapy market is expected to fall by US\$8bn (50 per cent) due to generic incursion on branded statin revenues Source: Datamonitor forecasts; patent data obtained from Dolphin, Q2 2006, © Thomson Scientific; FDA Orange Book; MedTRACK, © Datamonitor plc; all accessed during July 2006

that Lipitor was recovering lost ground by delivering growth in new and total prescriptions. Based on these assumptions, it is expected that US Lipitor sales will grow by 8 per cent between 2005 and 2006, and flatten out to grow by 1.6 per cent between 2006 and 2008.

IMPACT OF GENERIC INCURSION ON THE OVERALL STATIN MARKET

At the end of 2005, generics only accounted for around 10 per cent of the US statins market (MIDAS sales, IMS Health, March 2006). With both Zocor and Pravachol becoming exposed to generic competition in 2006, the balance is expected to move in favour of generics, with the sales volume and, indeed, the value, increasing over the next two to three years.

The most likely scenario in the statin monotherapy market in the US is a high level

of switching from Zocor to generic simvastatin, with a moderate level of switching from Lipitor to generic simvastatin. This is represented in Figure 2. Between 2006 and 2011, the value of the US statin monotherapy market is expected to fall by US\$8bn. Moreover, when Lipitor loses patent protection in the US in 2011, a further US\$6bn is likely to be lost as generic versions of atorvastatin experience strong uptake at the expense of the remaining branded statins and the generics already available in the market.

A MODEL FOR THERAPEUTIC SUBSTITUTION: WHAT WILL BECOME OF THE ANGIOTENSIN RECEPTOR BLOCKERS?

At the end of 2005, the US angiotensin receptor blocker (ARB) market, including sales of monotherapies and fixed-dose combination products, was worth US\$4.8bn,

with Datamonitor predicting this to peak in 2010 with sales of US\$7.2bn.⁹

In a similar fashion to the antidiyslipidaemics market, the second highest selling product of the ARB class, Merck & Co.'s Cozaar (losartan), will lose patent protection first in 2009, with generic losartan potentially having an impact on sales not only of Cozaar but also on sales of other leading ARBs, including Novartis's Diovan (valsartan) and AstraZeneca's Atacand (candesartan).

Datamonitor research has found that many key opinion leaders believe that prescribing habits will change, either voluntarily or via policies implemented by governments, when the ARBs begin to lose patent expiry in key markets such as the US in 2009, with one French key opinion leader stating that he believes that as soon as the ARBs begin to lose patent protection, there will be '...a mass exodus away from other classes, such as the ACEs, to generic ARBs'. As a result of a perception that ARBs are superior to other antihypertensive drugs due to their placebo-like tolerability, Datamonitor anticipates that the ARB market will actually grow in volume terms as patients are switched from other antihypertensive drug classes.

By observing the impact of generic simvastatin on the US antidiyslipidaemics market, and the rate of generic incursion on Zocor revenues, the key players in the antihypertensive market, such as Novartis and Merck, will be investigating new strategies to reduce the impact of generic erosion on key antihypertensive brands such as Cozaar and Diovan. A potential strategy would be the development of FDC products that treat one disease, an approach that Novartis is investigating with the development of Exforge (valsartan plus amlodipine). Another would be the development of FDC products that

address multiple cardiac risk factors, an approach that is also being employed by Novartis. Several patents exist for valsartan in combination with drugs that treat other cardiac risk factors, such as diabetes and high cholesterol.¹⁰ Owing to the less than impressive uptake of Pfizer's Caduet (atorvastatin plus amlodipine) in the US however, Datamonitor believes that the value of this strategy has yet to be proven.

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