

Switching patients from atorvastatin to simvastatin, and losartan to candesartan in a primary care setting: cost savings and clinical outcomes

Supported by
an unrestricted
educational grant
from Takeda UK Ltd

Supplement produced in association with  **Guidelines**
in practice

Switching patients from atorvastatin to simvastatin, and losartan to candesartan in a primary care setting: cost savings and clinical outcomes

Juliet Usher-Smith, Foundation Year 1 House Officer, West Suffolk Hospital, Bury St Edmunds; Professor Mike Kirby, Visiting Professor, Faculty of Health and Human Sciences, University of Hertfordshire; Hilary Pearmain, East and North Hertfordshire Primary Care Trust; and Tim Ramsbottom, General Practitioner, Letchworth, Hertfordshire

Introduction

Our primary care practice was asked by the local PCT to switch suitable patients from medication with atorvastatin to simvastatin, and from losartan to candesartan for the purposes of cost saving. At a pharmacological level, both switches involved changing between drugs with fundamentally similar modes of action: atorvastatin and simvastatin are both statins that decrease cholesterol by inhibiting the rate-limiting step in cholesterol synthesis; losartan and candesartan are both angiotensin receptor blockers (ARBs) used in the treatment of hypertension.

While there is substantial evidence to support the relative clinical effectiveness of these drugs, this is mostly from case control studies comparing two or more drugs in different patient groups. There is little literature following through the relative effectiveness in individual patients. We, therefore, took the opportunity to assess the clinical, practical, and cost implications of switching to generic drugs.¹ We used total serum cholesterol and clinic blood pressure readings, together with feedback from patients and analysis of time and cost, to assess the overall impact of switching patient medications on both an individual and practice level. Additionally, by performing both switches at the same time, we were able to compare the relative outcomes and highlight some of the issues specific to each class of drug.

Identification process

We began by searching the practice computer records to identify all patients currently being prescribed either 10 or 20 mg atorvastatin or any dose of losartan. The practice support pharmacist then carried out preliminary screening on the selected patients. Patients on atorvastatin were excluded if they:

- had a total cholesterol >5 mmol/l on a 10 mg dose or >4.6 mmol/l on a 20 mg dose
- had a previous history of simvastatin use that had failed to reduce their cholesterol to target
- were also taking warfarin or amiodarone
- had chronic renal failure or a history of organ transplantation.

These criteria were chosen because it was felt that it would not be appropriate to switch those patients who had either failed to reach or who were only just below target on atorvastatin, or those who had been switched to atorvastatin from simvastatin in the past because of a failure to reach target levels for cholesterol. Simvastatin, but not atorvastatin, also requires caution to be exercised when prescribed at doses above 10 mg in people with renal impairment, and special dosing considerations when used with a number of drugs, including warfarin or amiodarone. Patients taking losartan were also screened by the pharmacist but were only excluded if there was no evidence of prior angiotensin-converting enzyme inhibitor (ACEI) use, in which case they were switched to the ACEI ramipril.¹ This was possible because both losartan and candesartan are licensed for the treatment of hypertension.²

The remaining records were then reviewed by their registered GP to identify additional medical conditions, or administrative and social reasons that would make them unsuitable for switching medication. Those patients identified as suitable for switching were then sent a letter informing them of the proposed change to their medication and asking them to contact their doctor if they had any concerns. The repeat prescriptions for all these patients were then changed so that, unless they contacted the surgery, they would automatically receive the new drug.¹ Tools and resources that may be useful when conducting a switch programme are listed in Box 1 below, and brief practical guidance on how to implement a switch programme is highlighted in Box 2 overleaf.

Box 1: Tools and resources to assist with a switch programme

- Get help from the pharmacist adviser
- Make use of the GP's knowledge of the patients
- Exploit the valuable IT resources to check previous concordance from repeat prescriptions, and subsequent concordance
- Use personnel in the practice in a cost effective way; for example, encourage healthcare assistants and/or practice nurses to assist with the programme.

Box 2: Practical guidance on how to implement a switch programme

- Review the patients carefully
- Provide clear written instructions to the patients
- Offer telephone consultations
- Check concordance
- Follow-up readings and test results within 3 months
- Check whether patients are on other medications like aspirin and warfarin
- Take the opportunity to review other current medication
- Remember that there is a cost implication to the practice for the first year of the switch.

The records of those patients switched were reviewed at that time for baseline cholesterol or blood pressure measurements and then again 3–4 months after the switch. Those who had not already had a serum cholesterol measurement taken or blood pressure recorded during routine clinical care since the switch were contacted and invited to attend the surgery. Patient records were then reviewed again 10 months after the switch to look for new diagnoses of ischaemic heart disease or cerebrovascular accidents within each group.

Calculating equivalent doses

Patients were switched to doses of simvastatin and candesartan that have been shown to be approximately equivalent to their current doses of atorvastatin and losartan.^{3–8} For the statin switch, the CURVES study compared the mean percentage change in low density lipoprotein cholesterol for a range of statins and showed that 10 mg atorvastatin is approximately equivalent to 30 mg simvastatin.³ Together with the Heart Protection Study, which provided reliable evidence about the safety of 40 mg simvastatin,⁹ this has led to a growing consensus that all patients taking either 10 or 20 mg atorvastatin should be switched to 40 mg simvastatin. At the time of this study, however, we chose to switch all patients already on 20 mg atorvastatin as well as those on 10 mg atorvastatin for secondary prevention to 40 mg simvastatin, and those on 10 mg atorvastatin for primary prevention to a 20 mg dose of simvastatin. All patients on losartan were switched to 4 mg candesartan for each 25 mg dose of losartan.

Key findings

Atorvastatin to simvastatin switch

For the statin switch, 122 patients were identified as currently being prescribed atorvastatin 10 or 20 mg. Of these, 43 patients were excluded by the practice pharmacist and a further nine by the GPs. The most common reasons

for exclusion were inadequate cholesterol control, a known intolerance to simvastatin, or a history of previous simvastatin use with failure to reach cholesterol targets. Letters were sent to the remaining 70 patients. None of them responded and so all 70 were subsequently switched to simvastatin. Of these, one patient switched back as a result of side-effects but 69 out of the original 122 were successfully switched to simvastatin.

Cholesterol readings taken before and after the switch were obtained for 61 of the 69 patients switched. Figure 1, page 5, shows the individual total cholesterol readings for each of these patients at both time points. The mean total cholesterol for all patients was 4.07 ± 0.55 mmol/l prior to the switch and 4.10 ± 0.73 mmol/l after the switch. Not only did these mean values not change, but analysing the data using a paired Student's t-test, to take into account changes in each individual, showed that there was no statistically significant difference between the total cholesterol levels before and after the switch.

Review of the three different dosage groups showed that, although again the changes were not significant, the total serum cholesterol in those patients switched from 10 mg atorvastatin to 20 mg simvastatin, and from 20 mg atorvastatin to 40 mg simvastatin increased slightly after switching. By contrast, those patients who were switched from 10 mg atorvastatin to 40 mg simvastatin showed a slight decrease in total cholesterol level. This is consistent with findings from the CURVES study, which demonstrated that a dose of 10 mg atorvastatin was approximately equivalent to a dose of 30 mg simvastatin.³ We therefore recommend that 40 mg simvastatin is the dose of choice for patients previously on either 10 or 20 mg atorvastatin. It is not appropriate to switch patients who are currently on higher doses of atorvastatin, according to results of a recent audit performed in a secondary care setting.¹⁰

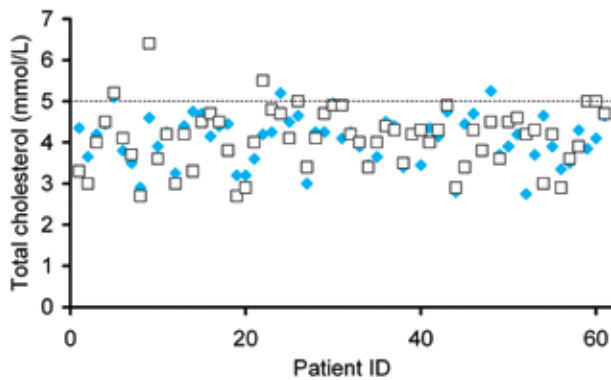
Although our study was not long enough or sufficiently powered for all clinical outcomes, 10 months after the medication switch there were no new diagnoses of ischaemic heart disease, nor cerebrovascular accidents among these patients. We plan to follow the patients up again 2 years after the switch, which will provide more long-term outcome data.

Losartan to candesartan switch

For this switch, a total of 137 patients were identified as currently being prescribed losartan. Of these patients, five were excluded by the pharmacist, three for having no history of ACEI use who were switched to ramipril instead, and two who had recently had their losartan dose stopped by secondary care. A further 11 were identified by the GPs as being unsuitable for switching, mostly for administrative and social reasons, which contrasts with the statin switch where the majority were excluded for reasons connected with their cholesterol levels.

Letters were sent to the remaining 121 patients, six of whom requested not to switch, and several were very unhappy at

Figure 1: Total cholesterol before (closed diamonds) and after (open squares) switching from atorvastatin to simvastatin (the dotted line marks the audit standard)¹



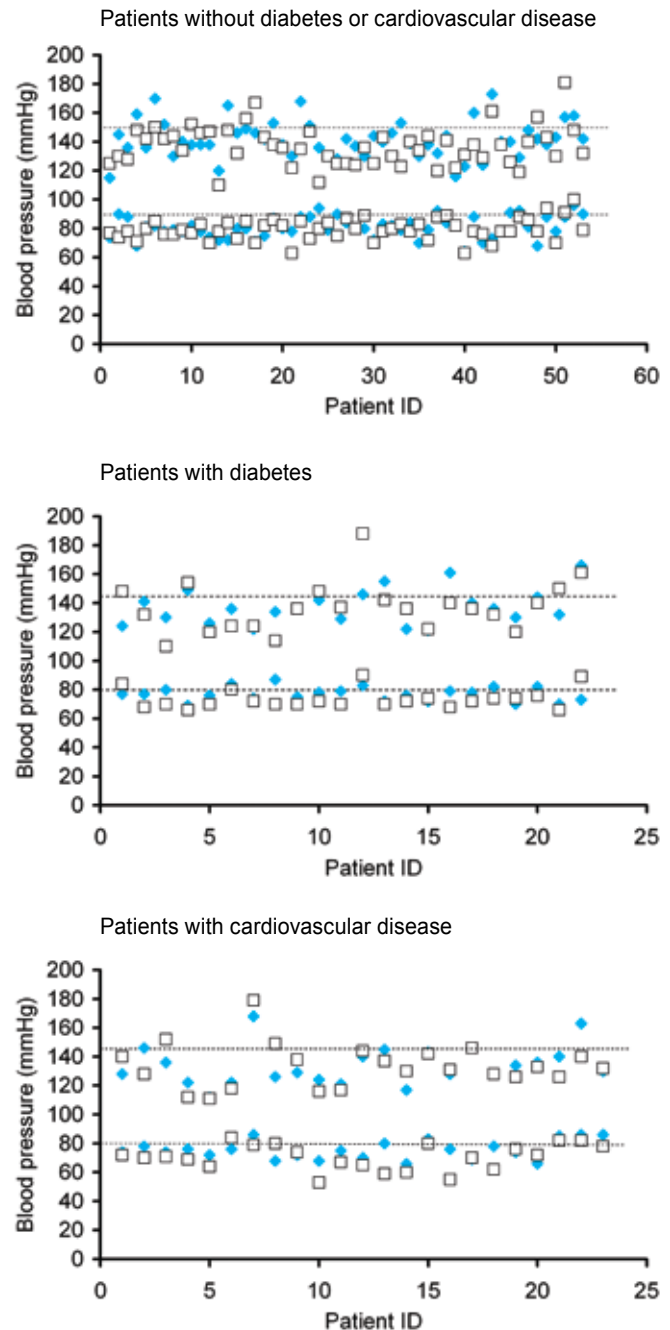
Adapted from Usher-Smith J et al. *Int J Clin Pract* 2006; **61** (1): 15–23. Reproduced with permission.

having been asked to switch. However, 115 patients were switched to doses of candesartan. Of these, seven patients subsequently switched back but, with the exception of one patient who switched back to losartan after 7 months as a result of poor blood pressure control, these were all for rather non-specific reasons unlikely to be related to the medication. This, together with the six patients who requested not to switch, again contrasts with the statin switch where all patients were switched and only one changed back for reasons of recognised side-effects. This difference in attitude may reflect the fact that current guidelines in the UK only recommend use of an ARB if first-line treatment with an ACEI is not tolerated. Patients who are prescribed a sartan have, therefore, already undergone at least one switch in their treatment for hypertension and, in many cases, several. Nevertheless 108 out of the original 137 were successfully switched from losartan to candesartan and blood pressure measurements taken before and after the switch were obtained for 98 of these 108 patients.

In these 98 patients there was a small but significant ($p=0.0006$) reduction in blood pressure after the switch ($138.9/78.7 \pm 13.2/7.0$ mmHg to $136.3/76.1 \pm 14.7/8.4$ mmHg). In accordance with the British Hypertension Society guideline for blood pressure control,¹¹ we subdivided these patients into those with diabetes (audit standard $<140/80$ mmHg), those with a history of cardiovascular disease (audit standard $<140/80$ mmHg) and those without either diabetes or a history of cardiovascular disease (audit standard $<150/90$ mmHg). The blood pressure measurements of all patients in those three groups taken before and after the switch are shown in Figure 2.

A review of the patient records 10 months after the switch revealed that one patient with diabetes had suffered a lacunar infarct and a further mild right hemispheric stroke. However, his blood pressure at that time was comparable to that before the switch and it is, therefore, unlikely that these events were directly attributable to the change in medication.¹

Figure 2: Systolic and diastolic blood pressure recordings before (closed diamonds) and after (open squares) switching from losartan to candesartan (the dotted lines indicate the audit standard)¹



Adapted from Usher-Smith J et al. *Int J Clin Pract* 2006; **61** (1): 15–23. Reproduced with permission.

Cost savings

Financially, both switches generated substantial savings for the practice. The total saving in drug costs per annum for the 69 patients successfully switched to simvastatin was £14,712.88. The one-off cost for the switch itself, including the time spent by the pharmacist and GP screening the patients and the postage and additional appointments, was £1997.30. The net saving to the practice this year was, therefore, £12,715.58. The patent for atorvastatin does not

Key learning points from the study

- Switching drugs in primary care can be safe, and in some cases even clinically beneficial for patients, but it requires very careful patient selection—when switching from atorvastatin to simvastatin, up to 50% of patients may be unsuitable for switching (based on our study)
- Inappropriate drug switches have been shown to cause adverse events.¹⁰ We found that a small minority of patients switching from losartan were unhappy at being asked to change, and these patients might require additional follow-up
- Good communication with the patients is important—this makes them less likely to stop taking their medication and, in turn, decreases the chance of patients having an adverse event that could negate any financial benefits of the switch
- This study showed that switching medication was cost effective—the net annualised savings for the year 2005–2006 were £12,715.58 for the statin and £13,374.40 for the antihypertensive switch, respectively
- When making an assessment of future financial savings it must be remembered that the cost of drugs is not fixed, and companies may subsequently change the price, as in the case of losartan.

expire until November 2011 and so over the next 5-year period this would translate into a saving of over £70,000.¹

Similar savings were seen with the sartan switch. The total saving in drug costs per annum, was £14,008.67, and with a one-off cost of £634.27 this gave a net saving to the practice this year of £13,374.40. The patent for losartan will expire in September 2009, while that for candesartan remains valid until April 2012, so this significant saving will only continue until September 2009. This raises issues about the ethics of continually chasing cost savings as the prices of drugs change. However, in the 2-year period since the switch this has translated into a saving of over £27,000.

Both switches were, therefore, very cost effective and if implemented throughout individual primary care practices could generate substantial savings for PCTs. It is important to remember, however, that there was a significant financial cost to the practice of performing the switch, and the number of patients excluded highlights the importance of carefully reviewing patients and not switching patients inappropriately.

2007 update

In August 2007, the price of losartan was decreased so that at current pricing 8 mg candesartan costs 23% less than 50 mg losartan, and 16 mg candesartan costs 21% less than 100 mg losartan. This reduces the annual saving in our practice from £14,008.67 to £5,324.05 and highlights the fact that any switch performed for cost-saving purposes is dependent on the market and so the saving is unpredictable.

References

1. Usher-Smith J, Ramsbottom T, Pearmain H, Kirby M. Evaluation of the cost savings and clinical outcomes of switching patients from atorvastatin to simvastatin and losartan to candesartan in a primary care setting. *Int J Clin Pract* 2006; **61** (1): 15–23.
2. Amias[®] Summary of Product Characteristics. Takeda UK Ltd. November 2006.
3. Jones P, Kafonek S, Laurora I et al. Comparative dose efficacy study of atorvastatin, pravastatin, lovastatin, and fluvastatin in patients with hypercholesterolemia (the CURVES Study). *Am J Cardiol* 1998; **81** (5): 582–587.
4. Nishimura T, Hashimoto J, Ohkubo T et al. Efficacy and duration of action of the four selective angiotensin II subtype 1 receptor blockers, losartan, candesartan, valsartan and telmisartan, in patients with essential hypertension determined by home blood pressure measurements. *Clin Exp Hypertens* 2005; **27** (6): 477–489.
5. Lacourcière Y, Asmar R. A comparison of the efficacy and duration of action of candesartan cilexetil and losartan as assessed by clinic and ambulatory blood pressure after a missed dose, in truly hypertensive patients. *Am J Hypertens* 1999; **12** (12 pt 1–2): 1181–1187.
6. Baguet J-P, Nisse-Durgeat S, Mouret S et al. A placebo-controlled comparison of the efficacy and tolerability of candesartan cilexetil, 8 mg, and losartan, 50 mg, as monotherapy in patients with essential hypertension, using 36-h ambulatory blood pressure monitoring. *Int J Clin Pract* 2006; **60** (4): 391–398.
7. Conlin P. Angiotensin II antagonists in the treatment of hypertension: more similarities than differences. *J Clin Hypertens* 2000; **2** (4): 253–257.
8. Jones P, Davidson M, Stein E et al. Comparison of the efficacy and safety of rosuvastatin versus atorvastatin, simvastatin, and pravastatin across doses (STELLAR[®] Trial). *Am J Cardiol* 2003; **92** (2): 152–160.
9. HPS Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet* 2002; **360** (9326): 7–22.

-
10. Butler R, Wainwright J. Cholesterol lowering in patients with CHD and metabolic syndrome. *Lancet* 2007; **369** (9555): 27.
 11. Williams B, Poulter N, Brown M et al. The BHS guidelines working party guidelines for management of hypertension: report of the fourth working party of the British Hypertension Society, 2004—BHS IV. *J Hum Hypertens* 2004; **18** (3): 139–185.

This supplement has been supported by an unrestricted educational grant from Takeda UK Ltd.

The content of this article is independent of the commercial support and editorial control has remained with the author and *Guidelines in Practice*.

The views and opinions of contributors expressed in this publication are not necessarily those of Takeda UK Ltd, Connectmedical or of *Guidelines in Practice*, its publisher, advisers and advertisers. Full editorial control has remained with the authors and *Guidelines in Practice*.

No part of this publication may be reproduced in any form without the permission of the publisher.



Produced by Connectmedical, a division
of Medendium Group Publishing Ltd