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Perceptions of generic medicines and the cost-benefits of generic switches

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Perceptions of generic medicines and the cost-benefits of generic switches

This is the second article in the mini-series on generic medicines. Here, we focus on the perceptions of patients and healthcare professionals on generic products, with some valuable insight provided by Gail Chan, Team Leader for a Practice-based Commissioning (PBC) Group in Liverpool and Medicines Management Team Leader for Diabetes. A brief outline of the main events surrounding loss of patent protection and important cost considerations for commissioners of pharmaceuticals will also be given.

Introduction

We began this series with an article that looked at current debates and policies in developments relating to generic substitution, including the recent Government consultation on generic substitution, the implementation of which is hoped to increase productivity and reduce drugs spending.[1] Several concerns with the introduction of generic substitution have been raised in the literature, including worries that '*generic* substitution could be the first step on the road to *therapeutic* substitution'[2] (see Box 1). Other points raised are that 'therapeutic switches are time consuming, incur financial costs and may cause significant irritation to patients'.[3] There are also concerns about reduced compliance,[2,4] attribution of legal responsibility if an error occurs or harm befalls a patient, and patients' perceptions.[2] This article looks in more depth at healthcare professionals' views on generic substitution and generic switch policies and considers the costs and potential savings of switching from branded to generic products.

Box 1. Generic and therapeutic substitutions

Generic and therapeutic substitution can have different clinical implications.

Generic substitution: The generic product has the same pharmaceutical form and strength as the branded product and its active substance has the same rINN or BAN as the branded product or is a permitted alternative salt of the reference product with an INNM or BANM, which relates to the rINN or BAN for the branded product, unless the rINN covers the salt.[1]

A generic substitute is, therefore, expected to be broadly chemically equivalent to the branded product (but it should not be assumed that all generics are identical because different excipients could exert distinct effects.[6,7,8]

Therapeutic substitution: This involves substituting the branded product with a generic product from the same therapeutic group or class.[2] It may not necessarily, therefore, have identical clinical indications, mode of action, interactions with co-medication and adverse effects as the reference branded product.

Key: rINN = recommended International Nonproprietary Name; BAN = British Approved Name; INNM = INN Modified; BANM = BAN Modified

Patent expiry to generics availability

In an ideal world at a branded drug's patent expiry, information about the likely time-course of a generic entry and cost-decay curves for both branded and generic products would be available at the 'touch of a button'. In reality, however, this is a very complex area and subject to various impacting influences. A brief overview of the main processes involved in the production and marketing of a generic alternative to a branded product may help understand how some of these factors can influence the speed with which generics can be made available after a patent expiry and their potential entry price.

Thomson Reuters recently undertook research aimed at exploring issues around generic competition. It found the earliest and most reliable signal of future generic competition is the activity of companies manufacturing generic active pharmaceutical ingredients (APIs) because without a source of quality generic API, a generic finished product can never be a reality in regulated markets.[5] In fact, most generic companies work to similar development timelines as originators – typically around 8–10 years – actively examining drugs for future development as soon as they have been approved or launched depending on the anticipated commercial potential of the compound, the readiness of a reliable source of the generic API, patent protection and exclusivities.[5]

Manufacturer inspections are essential

In the UK, the Medicines and Healthcare products Regulatory Agency (MHRA) is the body responsible for inspecting manufacturers of APIs whenever a company has applied for or has been named on an appropriate

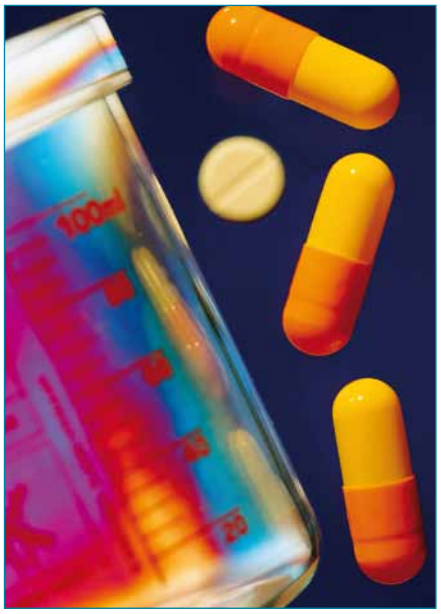
licence to ensure that medicinal products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorisation or product specification.[9] Medicines may be licensed for use in the UK either on a national basis (directly through the MHRA), through a centralised approval system of the European Medicines Agency (EMA) or through a procedure for 'mutual recognition'. Under the centralised scheme, companies apply for a licence directly to the EMA. Under the mutual recognition procedure a company may designate one EU country to approve a drug licensing application, and then receive marketing authorisation in various EU countries, provided these other countries agree.[10,11] A further scheme, the decentralised procedure, operates in which companies may apply for simultaneous authorisation, in more than one EU country, of products that have not yet been authorised in any EU country and that do not fall within the mandatory scope of the centralised procedure.[11]

Regulatory standards must be met

Regulatory standards for safety and efficacy are the same for generic medicines as for branded products and marketing authorisation must be obtained from the MHRA before a drug is allowed on to the market in the UK.[10] The approval to market a medicinal product is based on the evaluation of scientific data provided by the company to support its quality, safety and efficacy.[12] If a 'new' product contains drugs which have been previously well-tested and approved in other forms or for other companies, then European Directives (in particular Directive 2001/83EC) allow for what are known as 'abridged' applications (for marketing authorisation), so that companies do not have to unnecessarily repeat the tests and trials on animals and humans.[12] If the new product meets requirements for a generic product (defined in the European Directive), then it can be authorised without its own clinical and pre-clinical testing data.[12]

Proving generic equivalence with branded products

The EMA requires a generic product to have the same qualitative and quantitative



composition in active substances and the same pharmaceutical form as the reference product, and to show bioequivalence in pharmacokinetic measures to it.[13] For the generic and reference product to be accepted as being bioequivalent the 90% confidence interval for the ratio of the generic and reference products should be within the acceptance interval of 80–125%.[13]

> 'Not all drugs within the same therapeutic class are interchangeable with respect to outcome.'[8]

These boundaries of acceptable variability have been regarded as being too wide in some cases,[14] in particular, they should be reduced when an active principle displays a narrow therapeutic range (the so-called critical-dose drugs) such as immunosuppressants (eg ciclosporin), anti-epileptics and anti-coagulants.[8,13] Clinical or therapeutic bioequivalence, implying the same effect of two products, is not measured in bioequivalence studies[8] and is not, therefore, a pre-requisite for making a substitution.[15] However, once the bioequivalence conditions are met and the abridged marketing authorisation is granted the generic product could be sold in the UK.

Suitability of generic substitution

Perhaps the main criticism of data obtained from bioequivalence studies is that the conditions under which the testing is performed 'may not be (fully) relevant to the practical situation' as these are often performed on normal, healthy and relatively young volunteers.[8] This could lead to some patients being put at risk of reduced efficacy and/or increased risk of adverse events.[15] Patients in clinical practice could be elderly with several co-morbidities and subjected to poly-pharmacy for the treatment of hypertension and/or ischaemic heart disease, for example, such that extrapolation of bioequivalence data may not be justified.[8] Even if the generic and branded products are chemically equivalent, a difference in excipients could lead to a distinct therapeutic and safety/tolerance profile.[8]

Similarly, not all drugs within the same therapeutic class are interchangeable with respect to outcome.[8] For example, all anti-hypertensive drugs are licensed on the basis that they lower blood pressure (BP) and it is assumed that for any given identical BP reduction they will be equivalent by way of influencing hard endpoints, ie reducing the risk of (non-) fatal stroke, myocardial infarction (MI) and heart failure.[8] However, consideration should be made to the additional approved licensed indications for some angiotensin II receptor blockers (ARBs) (Table 1). While some ARBs have further licensed indications, others (eprosartan[16] and olmesartan[17]) are purely licensed for uncomplicated hypertension. Pressures to reduce spending and to instigate proactive switch policies will need to take careful account of clinical need and suitability of the generic product for each patient as described in Box 2.

For Gail Chan, Medicines Management Team Leader for PBC Groups across Liverpool and Clinical Lead in Diabetes, prescribing generics *per se* is not a major concern because general practitioners (GPs) in her practices *"prescribe generics anyway, so the patients are used to receiving them and don't worry about them"*. In general, Gail says that *"differences in bioavailability between generics does not cause problems, although*

there are some well-known exceptions", which GPs and community pharmacists (CPs) will bear in mind. Also *"it is essential to prescribe by brand slow-release formulations and some drugs with narrow therapeutic indices"*, adds Gail. Although generic prescribing causes few problems, *"therapeutic substitutions where products may have different indications are trickier and could lead to more complications"*, says Gail. *"For example, any ARB would be ok if a patient only had essential hypertension"*, she explains, *"but if a patient also had heart failure and was given a different ARB to the usual one, then perhaps this could lead to problems"*, emphasising the importance of prescribing drugs with appropriate licensed indications.

"Differences in bioavailability between generics does not cause problems, although there are some well-known exceptions… substitutions where products may have different indications are trickier and could lead to more complications." Gail Chan

Perceptions about generic prescribing or substitution

There are some published studies of patients' attitudes towards generic drugs and generic substitution and some evidence

to show that both patients' and healthcare professionals' perceptions can influence acceptance of generic medicines.

Healthcare professionals' perceptions

The statistics showing an average generic prescribing rate in excess of 83% in the UK primary care sector[1] suggests that the principle of prescribing appropriate generic products is generally acceptable to GPs and prescribers. The proposed generic substitution, however, essentially means that a pharmacist could overrule a prescribing decision and this has raised some general worries among a new community pharmacy 'think tank' – *Chemists and Druggists* (C+D) Senate.[4] For instance, examining prescriptions for generic substitution might increase workloads, taking valuable time away from other important projects[4] such as initiatives to improve compliance, which might bring a better return in terms of time or investment cost.[4] The C+D Senate also raised concerns about how the public will view pharmacists and how GPs might react.[4] Although unfounded on experience it has been suggested that the public might perceive generic substitution simply as a means of generating income for community pharmacists.[4]

Although there is little published on prescribers' perceptions of generic substitution, emphasis is generally placed upon the appropriateness of the generic and patient safety where switches have been dictated by policy.[18] Similarly, concerns for patient welfare underpinned a worry expressed at a C+D Senate meeting that there is a need for pharmacists to be allowed to opt out of making substitutions without being penalised, particularly where in their clinical judgement this would not be in the patient's best interests.[4] Allan Tenant of the Dispensing Doctors' Association (DDA) also noted concern that primary care trusts (PCTs) could interpret the Government guidance (on generic substitution) as being mandatory, although this is not what it intended and raised the issue of a need to determine who would be responsible if a patient came to harm following a generic substitution.[2]

Table 1. ARB licensed indications in addition to essential hypertension and patent expiry dates

Angiotensin II receptor blocker	Expected patent expiry	Licensed indications in addition to essential hypertension
Losartan (Cozaar)	Expired March 2010	Treatment of renal disease in adult patients with hypertension and type 2 diabetes mellitus with proteinuria 0.5 g/day as part of an anti-hypertensive treatment. Treatment of chronic heart failure in patients >60 years old, when treatment with angiotensin-converting enzyme inhibitors (ACEIs) is not considered suitable. Reduction in the risk of stroke in adult hypertensive patients with left ventricular hypertrophy documented by electrocardiogram.[22]
Valsartan (Diovan)	May 2011[3]	Treatment of clinically stable patients with symptomatic heart failure or asymptomatic left ventricular systolic dysfunction after a recent (12 hours–10 days) MI. Treatment of symptomatic heart failure when ACEIs cannot be used, or as add-on therapy to ACEIs when beta-blockers cannot be used.[23]
Candesartan (Amias)	April 2012[3]	Treatment of patients with heart failure and impaired left ventricular systolic function (left ventricular ejection fraction 40%) as add-on therapy to ACEIs or when ACEIs are not tolerated.[24]
Irbesartan (Aprovel)	August 2012[20]	Treatment of renal disease in patients with hypertension and type 2 diabetes mellitus as part of an anti-hypertensive regimen.[25]
Telmisartan (Micardis)	January 2014[21]	Reduction of cardiovascular morbidity in patients with atherothrombotic cardiovascular disease (history of coronary heart disease, stroke, or peripheral arterial disease) or type 2 diabetes mellitus with documented target organ damage.[26]

Patients' perceptions

Because of the possibility that negative attitudes to generic drugs might result in more practice visits, emergency consultations and additional hospitalisations, patients' attitudes and experiences towards generic drugs have been explored.[19] In one study 804 consecutive patients were recruited during 1 week from 31 randomly-selected practices in Germany and were surveyed about their knowledge of, and experiences with, generic drugs, and whether they felt appropriately informed about generic drugs and substitutions by their doctor.[19] Nearly two-thirds (509/804) stated they knew the difference between brand-name and generic products, but one-third of these were not satisfied with the information given by their GPs and 36.7% (295/804) considered inexpensive drugs to be inferior to, or different from, brand-name products.[19] People who expressed scepticism about generic substitution were more often among those who did not feel well-informed about the substitution by their doctor.[19] Of those patients who had some experience of generic substitution, 12–13% reported a lower efficacy or side-effects,[19] which perhaps influenced their opinions. A negative view of generic drugs was more often expressed by older people, and independently, by chronically ill patients[19] and the authors felt that these patients and those regularly taking several drugs will need consultation time with their GP to help allay any fears they have and better prepare them for switching medicines.[19] This point was underlined by Gail Chan, who believes it is important to provide patients with clear information up front in advance of any proposed medication changes because *"this makes it easier for patients to understand that the medicine isn't changing – simply the physical appearance and manufacturer'*, she says. *'Providing we explain the rationale and benefits of switching to generics most patients are happy with switching"*, she explains.

Usher-Smith and colleagues also emphasised the importance of communication with patients[27] and that the effectiveness of switching medications depends on the attitudes of patients and management of the switch.[28] They suggested that it is possible that attitudes towards switching medication will vary with the disease being treated, either because of the inherent nature of the condition itself or because of the number of drug changes already required in the past.[28]

The question of whether less expensive drugs would be perceived as being less effective by patients was explored in a US double-blind, randomised, pain-tolerance trial, in which healthy subjects were given a placebo 'opioid' and were informed that it was similar to codeine but had a faster onset of action and was either full price or discounted.[29] The findings showed that the tablets that were believed to be discounted by the subjects proved less effective than the regular price tablets, consistent with phenomena of commercial variables affecting quality expectations and expectations influencing therapeutic efficacy.[29]

There is a paucity of trial data in this area, but concerns have been raised in the literature about the potential for changing generics' packaging[2,15] and/or tablet appearance,[2] which could change with each repeat prescription, might be a source of anxiety[15] or confusion[2,15] for patients, especially the elderly.[2,15] This could also lead to a non-intentional reduction in compliance, although compliance is known to be particularly poor in the elderly and those with cognitive[2,30] or psychological[31]

Box 2. Factors to consider before making a generic or therapeutic substitution

Match generic indications to patient diagnoses

This will help to ensure that the licensed indications of any intended medicine or substitution are an appropriate treatment for the patient. For example, only two ARBs have an additional licensed indication for treating renal disease in patients with type 2 diabetes and hypertension: irbesartan[25] and losartan.[22] Trials with irbesartan demonstrated renal protection in both early and late stages of renal disease,[32,33] and losartan demonstrated protection in late-stage renal disease (protection in early-stage renal disease has not been investigated).[34] Similarly, losartan is indicated in chronic heart failure (in patients >60 years), when treatment with ACEIs is not considered suitable due to incompatibility[22] and candesartan in heart failure and impaired left ventricle systolic function (left ventricular ejection fraction 40%) as add-on therapy to ACEIs or when ACEIs are not tolerated.[24]

Evaluate patient-specific factors

Problems with generic substitution are more likely to occur in the presence of co-morbidities and/or polytherapy, and in elderly patients who may be liable to become confused by a medicine switch[2,30,31] and whose ability to absorb[35] or metabolise drugs may differ from the bioequivalence study population.[14] Patients' views should be sought; a minority of patients may be poorly compliant and reluctant to change[31] or may be against switching their medication.[27] For example, because current guidelines recommend use of an ARB only if treatment with an ACEI is not tolerated,[27,36] people who are prescribed an ARB will have already undergone at least one switch of their treatment for hypertension[27] and might, therefore, be reluctant to undergo another. Alternatively, patients may be well-controlled and reluctant to change their medication.

Evaluate medicine-specific factors

Medicines that have a narrow therapeutic index (eg anti-epileptic drugs, warfarin, immunosuppressants, digoxin),[2,8,14] modified-release preparations and multi-ingredient medicines have been recommended to remain as branded products.[2]

Consider ethical issues

It is important to consider patients' rights to choose their treatments in discussion with their healthcare provider and to provide information to help them make treatment decisions.[37] Patient adherence is a key determinant of therapeutic efficacy and outcomes.[15] Therefore, respecting patients' preferences in this way is likely to impact positively upon concordance and help maximise adherence.

Discuss switching medicines with patients and provide information

Good communication with 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.[27] Provision of information to patients has been highlighted as being potentially able to reduce the number of patients who are dissatisfied with generic substitution,[19] and so it will be necessary to consider *who* will identify and inform suitable patients (eg GP, pharmacist, nurse or other healthcare professional), how this will be done (eg by interview or letter) and how much time will be needed to do this and secure patients' concordance before switching medication.

impairment. One way Gail addresses this is by having well-informed patients. She says her patients are always advised *"to remember the generic name of the medicine they take and to know why they are taking it. That way, they are in a better position to know that they have the correct tablet if, for example, they move GPs or CPs"*.

In summary, the literature points to familiarity with generics[19] and past experiences of switching[28] as having an influence on patients' acceptance of generics. However, beliefs that cheaper generics may be inferior to branded products[19] could also impact upon outcomes by influencing patient expectations.[29] Patient perceptions appear

to be positively influenced by information provision[19] and this is particularly important in those with chronic conditions, the elderly and those who are taking several medicines.[2,30,31]

In some cases a satisfactory substitution will perhaps consume an inappropriate amount of time with regard to the costs saved because some of the patients' attitudes or prejudices will be difficult to rectify.[19]

Cost implications of patent expiry

"Cost", says Gail, *"is perhaps the main benefit of making a generic substitution"*, because generics are generally cheaper than the branded alternatives. *"Having more than one version of a product is also useful in terms of being able to maintain continuity of supply – if a manufacturer is having difficulty in meeting demand, there are other available alternatives, for example. They also give CPs flexibility to purchase cost-efficiently and maintain their businesses"*, she says.

However, the cost-decay curve following patent expiry differs from one drug to another and is difficult to predict because it depends upon market-driven issues.[3] Predicting drug prices is a very complex area and subject to fluctuations depending upon, among other things, the number of (market-ready) competitor generic products with appropriate marketing authorisations at patent expiry. Even where generic entry does occur, this does not automatically mean that effective price competition will result[38] – generic versions may not necessarily be priced sufficiently competitively for substantial savings to be made over the branded products, particularly if there are purchasing incentives for branded relative to generic products. An attempt was made to model 5-year cost-consequences of switching ARBs and to determine the switch option that offered the best value for money in a context of changing price structures.[3] The author constructed a Markov model and applied dose-specific BP lowering and cost to a typical population with mild to moderate hypertension, assuming an equal BP lowering efficacy across the ARB class.[3] To estimate the projected prescribing costs of each ARB, the model was based on the cost-decay curve of ramipril, which after 8 months had reached 22% of its pre-expiry price and then levelled off. This was felt likely to be more comparable with the potential situation of the ARBs than that of simvastatin, which reached 25% of its branded price after 15 months, probably reflecting the extreme competitiveness of the large statin market.[3]

> 'The cost-decay curve following patent expiry differs from one drug to another and is difficult to predict because it depends upon market-driven issues.'[3]

When switching en mass hidden costs can erode savings

Because generic products are often cheaper than their branded equivalents, switching would appear to make economic sense providing a cost-saving on each prescription item. However, costs, such as the need to search patient records to identify for suitable patients, time cost for staff to perform patient reviews and consultations to ensure compliance is not jeopardised,[30] and essential tests to determine the patients' current clinical status and whether they are achieving target values,[28] can all reduce the anticipated savings. Patient follow-up and repeat tests after a switch may also eat into savings.

Losartan has now lost its patent protection and by August 2012 the patents for valsartan, candesartan and irbesartan will all have expired,[3,20] so what effect might this have on prescribing? Gail says that *"our focus is on getting the best value for money and so we must take advantage of any cost savings"*. *"But all switches must be made after careful consideration of actual cost-savings"*, says Gail. *"This means assessing the*

Being 'up front' with patients

Gail Chan believes in being "up front" with her patients about the need to save money where possible *"in order that funds may be released for other medical areas – for instance, to give patients the opportunity of having newer, more efficacious, but expensive drugs"*, which might otherwise be unaffordable. On the occasions when patients are to be switched from a branded to generic product for the first time Gail follows a standard switch protocol. This involves searching the practice database to identify suitable patients, having the GPs approve the patient list and the protocol, then contacting all patients by letter to inform them of the intended switch. The letter explains *"that the new tablet is cheaper than the old one and is the reason for the switch"* and *"that the new tablet has the same effect as the old one"*, says Gail. Patients can phone Gail's team to discuss any concerns they may have or to object to being switched, but *"most are happy to switch without problems"*, she says. *"Out of 100 patients identified, the GP might reject around 5 and 3–5 others might express concerns about switching"*, estimates Gail, but 90–95% will switch and most will remain taking generics, she added.

generic drug costs minus expenses, the need for patient follow-up appointments and patient monitoring, and being mindful of the fact that drug prices will fall after patent expiry". In the case of generic losartan availability she has no intention of recommending a wholesale switch from other ARBs for her patients, which she feels would be unproductive. *"Patents will expire for other ARBs within 1–2 years, and other ARBs have different licensed indications, so I don't see that there will be any cost-benefit of switching patients to the cheapest ARB in the time available"*, she explained. *"If a person's BP goes out of control, this can take several months to re-stabilise and once you consider costs of BP monitoring and appointment times alongside falling prices, it is certainly not a productive approach to keep switching patients each time the prices fall"*, she says. It seems more likely then, that significant long-term cost savings will be achievable with losartan, valsartan, candesartan and irbesartan simply because of their impending patent expiries, without the complications and costs associated with switching patients.

Impact of national incentives to switch to generics

National schemes, such as *Better Care, Better Value* indicators, aim to increase efficiency in PCTs' prescription costs and value for money by highlighting performance variations and where efficiency can be improved.[39] Current indicators are to increase low-cost prescribing of proton-pump inhibitors, lipid modifiers and drugs affecting the rennin-angiotensin system, specifically the ACEIs.[39] There is no indicator relating to low-cost ARBs, but will this be expected to change with the availability of generic losartan? Gail was unaware of any pending decision about any national directives on this, but speculated that *"if all sartans are similar prices, there would be no need for a BCBV indicator – after all, these are to help keep costs down".* In addition, she emphasised the national guidance is to use ARBs only in cases where patients are intolerant to ACEIs, which is up to around 20% of patients. She acknowledged that ARBs are also used in hypertensive patients with renal disease, but they have a much smaller market share than the ACEIs and she was unaware of any moves to change guidance to reflect the impending ARB patent expiries.

It is, therefore, important to try to balance the predicted cost of leaving well-controlled patients on their current regimen and allow market-driven cost adjustments to be made against the potential costs of making rapid therapy changes in the anticipation of short-term savings. If compliance is reduced by switching or if side-effects or intolerance to an 'inactive' ingredient occur, there is a risk of disease progression leading to future drug costs and possibly hospitalisation. Therefore, although the use of generic drugs can result in considerable cost savings indiscriminate switching should be avoided, particularly in high-risk patients. If switches are to be made, this should be carried out according to the best available evidence to ensure that there are no adverse consequences, such as the increased number of cardiac readmissions and deaths that followed a financially-driven policy to suspend evidence-based prescribing of high-dose atorvastatin to patients after MI or revascularisation in favour of generic simvastatin 20–40mg.[18] Similarly, switching patients each time prices fall is unlikely to be cost-effective long-term.

> *"But all switches must be made after careful consideration of actual cost-savings"*, says Gail Chan. *"This means assessing the generic drug costs minus expenses, the need for patient follow-up appointments and patient monitoring, and being mindful of the fact that drug prices will fall after patent expiry."*

Conclusions

Rationalising existing prescribing expenditure within primary care represents one of the few areas where UK health commissioners can make cost savings without overtly limiting access to routine care or incurring manpower reductions within health service providers.[3] Strained budgets are placing the National Health Service under ever more pressure to find savings wherever practical and possible. Using generic medicines as cheaper alternatives to branded drugs, where clinically appropriate, is a valid goal that could free up badly needed funds for other medical needs. As Johnston points out 'treatment decisions should be transparent and based on strong clinical evidence',[15] so ensuring the licensed indications of the generic substitute are appropriate for the patient will help ensure the switch is in the patient's best interest. Providing information about the generic medicine and gaining the patients' agreement with the switch is in line with Government policies giving patients the right to choose their treatments and have the necessary information to help them make treatment decisions,[40] and this is recognised as helping to maximise concordance.

When branded drugs lose their patent protection and generic products enter the market it is likely that drug prices will fall, but generic entry does not automatically trigger effective price competition.[38] It is therefore very important to consider all aspects of making a switch including the clinical circumstances of each patient, the licensed indications of the generic drugs, potential savings to be made from a switch, hidden costs that could be incurred, such as monitoring and GP appointments and the effect of unpredictable price reductions after patent expiry. The ethics of continually chasing cost savings as the prices of drugs change has been highlighted in the literature and the cost-benefits of switching from branded to generic products where the timeframe to patent loss for the branded products is short, as is the case for the ARBs is, at best, questionable – it is more likely that significant long-term cost savings will be achievable with the price reductions that usually follow patent expiries, without the complications and costs associated with switching to generics. Only by careful consideration of these factors can a rational decision about whether a switch is justified be arrived at.

The final article in this series will focus more closely on the ARB market.

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Adverse events should be reported. Reporting forms and information can be found at www.yellowcard.gov.uk.

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