

For personal use only. Not to be reproduced without permission of the publisher (editorial@gabi-journal.net).

# Payers endorse generics to enhance prescribing efficiency: impact and future implications, a case history approach

Brian Godman<sup>1,2,3</sup>, BSc, PhD; Mohammed Abuelkhair<sup>4</sup>, PharmD; Agnes Vitry<sup>5</sup>, PharmD, PhD; Shajahan Abdu<sup>4</sup>, MD; Marion Bennie<sup>6,7</sup>, MSc; Iain Bishop<sup>7</sup>, BSc; Sahar Fahmy<sup>4</sup>, PhD; Kristina Garuoliene<sup>8</sup>, MD, PhD; Harald Herholz<sup>9</sup>, MPH; Andrew Martin<sup>10</sup>, BSc, MPharmS; Rickard E Malmstrom<sup>11</sup>, MD, PhD; Professor Saira Jan<sup>12,13</sup>, PharmD, PhD; Ulrich Schwabe<sup>14</sup>, MD, PhD; Catherine Sermet<sup>15</sup>, MD; Peter Skiold<sup>16</sup>, MSc, PhD; Luka Voncina<sup>17</sup>, MD, MSc, Professor Lars L Gustaffson<sup>3</sup>, MD, PhD

**Introduction:** Pharmaceutical expenditure continues to rise driven by a number of factors including ageing populations and the continued launch of new premium-priced drugs. Increasing use of generics versus originators and patent-protected products of the same or related classes can help conserve valuable resources. However, concerns with their effectiveness and safety compared to originators as well as only limited introduction of measures to promote their demand in some countries have led to variable use among countries. Countries need to learn from each other to further enhance their prescribing efficiency.

**Study Objectives:** Firstly to review successful case histories from different countries, and secondly, raise awareness about potential pitfalls that could undermine the success of future measures in order to provide future guidance on conserving resources in relation to generics.

**Methods:** A narrative review of case histories selected by co-authors using a range of different approaches. Systematic reviews are published elsewhere.

**Results:** Twelve case histories were selected depicting both supply- and demand-side measures. These include Croatia where the introduction of additional measures helped reduce drug expenditure as well as debt whilst improving access to new medicines, Lithuania where recent reforms decreased pharmaceutical expenditure in 2010 whilst the number of prescriptions increased by 9% versus 2009; Scotland where despite a 6.2 fold increase in statin utilisation, multiple measures limited the increase in reimbursed expenditure to just 7% in 2010 vs 2001; Sweden where the introduction of monthly auctions for generics has helped lower prices; and the US where managed care organisations actively encourage cross therapeutic opportunities for generics substitution where the safety and efficacy of a generic drug is similar to a patent-protected product in the class or related class to conserve resources.

**Conclusion:** Payers across Australia, Europe, Middle East (United Arab Emirates), and US have introduced multiple measures to both enhance the prescribing of generics and obtain lower prices, with the result that they are increasingly able to take advantage of the availability of generics. However, due to growing pressures on healthcare resources, it is important that countries accelerate the sharing of lessons learned about which policies and new measures are most effective in controlling costs.

**Keywords:** Demand-side measures, generics, pharmaceuticals, pricing

## Introduction

There is increasing scrutiny over pharmaceutical expenditure in view of its greater growth compared with other components of health care [1]. Pharmaceutical expenditure currently accounts for up to 60% of total healthcare costs in some countries [2]. This increasing scrutiny has stimulated many reforms and initiatives to moderate future growth. These include measures to increase the prescribing of generics versus originators at lower prices than originators; other measures aim to increase the prescribing of generics versus patent-protected products in the same or related classes [3-18]. Our paper in the first issue of the *GaBi Journal* gave examples of the different supply- and demand-side measures that are being used by health authorities and health insurance agencies to achieve these aims [1]. The objective of these measures is to help maintain comprehensive health care, particularly in Europe where there is continued pressure

on resources, without prohibitive increases in taxes or health insurance premiums. One reason for the pressure on resources is the continued funding of new innovative premium-priced drugs. Additional measures stem from an increased volume of drugs being used due to stricter clinical targets, rising patient expectations and ageing populations [3-5, 8, 9, 11, 19].

In Europe, in order to receive market authorisation, generic medicines have to demonstrate they have the same qualitative and quantitative composition as well as the same pharmaceutical formulation and bioavailability, as the originator medicine [20-23]. In addition, there must be no prior intellectual property associated with the generic drug [20, 22, 23]. In view of this, payers typically assume that if two medicines have the same bioavailability they should have a similar therapeutic effect. This appears generally to be the case and applies even

**Author for correspondence:** Brian Godman, BSc, PhD, Department of Laboratory Medicine, Division of Clinical Pharmacology, Karolinska Institutet, Karolinska University Hospital Huddinge, SE-14186, Stockholm, Sweden, brian.godman@ki.se

Submitted: 13 September 2011; Revised manuscript received: 24 April 2012; Accepted: 6 May 2012

## REVIEW ARTICLE

when the generic drug is in the form of a different salt to the originator as well as different indications initially, as seen with generic clopidogrel [24]. Two recent comprehensive reviews illustrate this by comparing the outcomes between generic and originator drugs for the treatment of two widely different diseases [25, 26]. The first review considered treatments for epilepsy and found no evidence of association between loss of seizure control and treatment with at least three types of anti-epileptic drugs, one of which was phenytoin [25]. Similarly, the second review, which focused on the treatment of cardiovascular disease, did not demonstrate superiority in outcomes for originators compared to generic drugs [26]. This included drugs with a narrow therapeutic index such as propafenone and warfarin [26]. Therefore, generic medicines can help conserve valuable resources without compromising the quality of care [1, 3-6, 8, 13-17, 20, 27].

Many different measures and initiatives have increased prescribing efficiency in Europe, and are summarised in a previous edition of the *Gabi Journal* [1, 27].

These resulted in generic medicines in Europe comprising 50% of the volume of dispensed drugs but only 18% of the expenditure on drugs in 2006 [19, 28], leading to estimated annual savings of Euros 25 billion per year among the 27 nations in the EU [28]. Expenditure on generics in Europe was 21% in 2007, with the EU accounting for 30% of worldwide sales of generics in 2007 [28]. The extent of the savings is helped by estimated price reductions of between 30% to 90% for generics versus originator prices just prior to patent loss, with typically between 10 to 30 manufacturers competing to supply the different generic products in each market [20, 27, 28].

In the US, the prescribing of generics is also gaining ground. For example, published studies have consistently shown that among managed care organisations (MCOs) co-payment tier levels three and four are associated with decreased use of prescription drugs [29]. This even applies to patients with chronic conditions with higher morbidity and mortality such as diabetes, hypertension and hypercholesterolemia [29]. On the other hand, there is improved adherence to drug therapy if patients are prescribed generic drugs with typically the lowest co-payment levels—Tier One [29]. These findings [29] are further substantiated with recent research reporting that ‘dispense as written’ requests from physicians in the US, aimed at reducing generics substitution leading to higher co-payments, were again associated with decreased rates of prescription filling [30].

However, there are concerns with the effectiveness and tolerability of generics compared with originator drugs [3, 7, 24, 31-37], with some originator companies questioning the quality of generics as part of their marketing strategies to reduce the erosion of sales which follow patent loss [38]. Whilst these concerns typically only apply to a minority of situations [34, 36, 39], as demonstrated for instance by ‘dispense as written’ prescriptions only accounting for 2.7% of prescriptions written by physicians in the US [30], failure by health authorities, physicians and pharmacists to adequately address these concerns will mean reduced savings in reality [3-5, 17, 40]. Potential concerns

regarding the effectiveness and tolerability of generics, and associated reduced savings from lower utilisation rates, have stimulated health authorities and health insurance agencies to instigate new initiatives to address these concerns, see Tables 1, 2 and 3.

There are also concerns among payers at the considerable variation in the price of generics. These can vary up to 36 fold among European countries and India, and greater than 50 fold among developing countries, depending on the molecule [2, 4, 20]. The price differences are independent of the population size of the country or levels of income [10, 41], and are leading some countries to continually review their generics pricing strategies so as to enhance resource savings [3, 4, 7, 9-16]. There is also wide variation across Europe in the utilisation of generics versus patent-protected products in the same class or related class [4, 5, 8, 11]. Reducing this variation will likewise enable payers to conserve additional resources as generic drugs become increasingly available [4, 8, 12, 13].

In the future it is likely there will be further expansion in the manufacture and availability of generics, given the likely size of the market. For example, global sales of pharmaceuticals were estimated at US\$820 billion in 2009 [1]. However between 2011 and 2016, products with current sales of US\$255 billion per year are likely to lose their patents [42]. This is in addition to high volume products that have already lost their patents in the past decade including various proton pump inhibitors (PPIs), statins, selective serotonin re-uptake inhibitors (SSRIs) and angiotensin converting enzyme inhibitors (ACEIs), helping to conserve resources [1, 4, 5-9, 11, 16, 18, 43].

As a result of the burgeoning availability of generics, and the concerns outlined above, payers need to continue to learn from each other regarding potential additional measures to further conserve costs as resource pressures grow.

### Study objectives

The principal objective of this paper is to produce guidance on potential ways to conserve resources around the use of generics especially to payers of health care. To this end, this paper firstly reviews measures that have been successfully introduced in different countries; secondly, potential pitfalls that could arise. The latter needs to be heeded to optimise potential savings from the increasing availability of generics.

### Methods

This is a narrative review of case histories. There is no systematic review of initiatives to enhance the utilisation of generics at low prices since these reviews have already been undertaken and published elsewhere including those by the co-authors [4, 5, 8, 11, 18, 27].

The case histories have been selected by co-authors to meet the objectives of the paper rather than document a specific number of case histories from each continent. They have been divided into those predominantly concerned with supply-side measures, those predominantly discussing demand-side measures, those combining both approaches, and finally those where payers have not always been able to fully realise potential savings.

**Table 1: Selected successful country case histories principally dealing with supply-side measures**

**Croatia [8, 11, 13, 44, 45]**

- A) Measures to reduce price of generics, originators and patent protected-products in classes introduced in 2009 to conserve costs whilst increasing the number of new innovative products reimbursed included:
- The first generics priced at up to 70% of the average price in Italy, France and Slovenia
  - Maximum price for the second and subsequent generics – up to 90% of the price of last bioequivalent molecule reimbursed, with market forces after that driving prices down since patients have to pay the difference if they still wish a more expensive molecule than the current lowest priced referenced molecule (rare in practice)
  - Instigation of a new reference pricing system for existing drugs principally based on Defined Daily Doses (defined as ‘the average maintenance dose of a drug when used on its major indication in adults’) with reference prices (Anatomical Therapeutic Chemical Levels 3 and 4 – Disease area and class) based on the lowest priced products with a market share of at least 5% by expenditure during the preceding 12 months. Patients again pay the price difference for a more expensive product. Manufacturers can opt to lower prices of other products in their portfolio if price reductions for particular products are problematic for them
  - Prices recalculated annually to make sure these stay within established price limits
  - The maximum price for original breakthrough products is up to 100% of the average price in Italy, France and Slovenia; the maximum price for original me-too products is up to 90% of average price of equivalent drugs in Croatia
  - Strict controls of marketing activities including mandatory recording of all promotional expenses and financial transactions with physicians and limiting representative activity. Companies can be fined for abuse
- B) Outcomes
- Health insurance expenditure decreased by 13% from 1.7 billion Kuna to 1.5 billion Kuna (Euros 0.2 billion) first six months 2010 versus a similar period in 2009
  - Reduction of Fund’s arrears to pharmacies from 1.3 billion Kuna (Euros 173 million) to 1 billion Kuna (Euros 137 million).

**Germany [4, 8, 46-48]**

- A) Measures to enhance the prescribing and dispensing of generics in Germany during the past decade include:
- Abolishing patient co-payments if the reimbursed price of the dispensed generics is at least 30% below the current reference price
  - Potentially reducing or abolishing co-payments if physicians prescribe drugs that Sickness Funds have successfully negotiated contracts with pharmaceutical companies, which include both patent-protected products and branded generics
  - Enhancing the prescribing of generics through financial penalties for physicians not reaching agreed target levels for prescribing generics including biosimilars versus originators, alongside reduced prescribing of premium priced patented drugs and expensive me-too drugs in a class
- B) Outcomes
- The rebates, included those for patented drugs, amounted to estimated savings of Euros 1.3 billion for the Statutory Health Insurance Funds in Germany in 2010.
- However, despite these measures the reimbursed prices of generics can be appreciably higher in Germany than the UK, with the UK introducing measures to enhance transparency in the pricing of generics, see Table 1A. The methodology outlined in Table 1A estimated potential savings of over Euros 1.4 billion in 2010 for the 50 leading generic products, and Euros 5.0 billion for the total generics market, if prices in Germany were aligned to those in the UK.

**Sweden [7, 49, 50]**

- A) Current measures
- Compulsory generics substitution was introduced in Sweden in 2002 to conserve resources. The implementation, which helped reduce reimbursed prices of high volume generics to between 4 and 13% of originator prices before they lost their patents, was assisted by the monopoly on community pharmacists, which all belonged to Apoteket AB. Pharmacists were until 2009 obligated to dispense the cheapest multiple source product available at the local pharmacy.
- There were however occasions when prices of some generics rose from one month to the next. In addition, there is currently competition among community pharmacists in Sweden.
- As a result, the government commissioned TLV (Swedish Reimbursement Agency) in the late 2000’s to establish new regulations for the de-monopolised pharmacy market incorporating increased service levels and accessibility of pharmacies, without increasing the costs of medicines. Following this, all pharmacies since 2009 are obligated to offer patients the cheapest molecule *on the market* when there are substitutable generic medicines available. In return, pharmacies received Euros 1/ package extra in their retail margin when they dispense drugs subject to generics competition.

(Continued)

**Table 1: Selected successful country case histories principally dealing with supply-side measures (Continued)**

In addition under the new agreement, there are regular monthly auctions of potential prices for each generic drug. Quarterly auctions were considered but rejected due to concerns with breaching the European Transparency Directive. Under this new system, the manufacturer with the lowest price wins the auction. However, the chosen manufacturer for a respective generic drug must be able to supply the whole market for the entire period. Having the current cheapest product gives the pertinent manufacturer exclusivity to the market. This equates to approximately 70% of the total sales during the period and almost 80% if crossed prescriptions, i.e. medicines that are not interchangeable due to medical reasons, are included.

To overcome potential supply issues, pharmacies are allowed to dispense an additional two further branded generics of the molecule when the cheapest medicine is out-of-stock at the wholesaler. They also have a 15-day washout period to de-stock the previous month's cheapest generic drug if pertinent. Pharmacies cannot choose freely between the three products. However, they can only offer patients the next cheapest generic drug in exceptional circumstance such as when there are delivery problems.

#### B) Next steps and future refinements

Since 2009, TLV has also been charged with monitoring and supervising pertinent areas of the pharmacy market, i.e. evaluating if pharmacies have been following the regulations such as those relating to substitution and how this has impacted on the supply of generics, prices of generics and reduced fluctuations in practice. This will be reported shortly.

TLV is also currently reviewing their remuneration to pharmacists due to concerns with the existing level of remuneration to fully compensate pharmacists for spending time if needed with patients each month explaining that the different branded generic drug is in fact the same molecule as their prescription.

Where possible, each case history documents the measures undertaken as well as the outcomes. No set format has been used to document the measures undertaken as their nature varies by country depending on the current situation and circumstances. In addition, in some countries there is an iterative approach to successive reforms such as Australia.

Whilst this may represent a limitation to the study design, we have counter-balanced this by including as co-authors those directly involved in implementing the reforms. Consequently, we believe this approach provides the most comprehensive and accurate insight into the situation in the respective countries. This approach has worked well in previous publications [1, 3-11, 14-18], and is seen as preferable to obtaining information solely through interviews.

### Results

As discussed under methodology, selected case histories have been divided into those predominantly concerned with supply-side measures, see Table 1; those documenting predominantly demand-side measures, see Table 2; as well as those combining both approaches, see Table 3.

However, there have been situations where health authorities and health insurance agencies have failed to realise the full resource benefits from the availability of generics, although this is changing through the instigation of additional measures, see Table 4.

### Discussion

As can be seen in Tables 1 to 4, payers across Europe, Middle East (United Arab Emirates), Australia and the US have introduced a range of measures to try and enhance the utilisation of generics as well as obtain lower prices, in order to try and maximise the opportunity that generics provide for conserving valuable resources.

Successful supply-side measures include aggressive pricing of the generics as seen in Lithuania, see Table 3, as well as increased transparency in the pricing of generics to further lower generics prices. The latter is seen in the UK, see Table 3. As discussed, the situation in Lithuania, see Table 3, demonstrates that it is possible for European countries with small populations to obtain low prices for their drugs despite the rhetoric [10, 60]. As a result, this helps to continue providing access to drugs even though drug budgets are being cut. This is also seen in Croatia with their extensive range of principally supply-side measures, see Table 1, regarding the pricing of generic and other drugs for the molecule (ATC Level 5) as well as the class (ATC Level 3 and 4). The various measures in Croatia helped engineer sufficient budgetary space to reduce the budget arrears to pharmacies as well as increase the availability to new drugs [13].

The monthly auction for generics prices in Sweden is a novel approach, which can potentially be transferable across countries. However, more analysis needs to be undertaken before this can occur, see Table 1. The specific contracting between pharmaceutical companies and individual sickness funds in Germany is also an interesting development, see Table 1. However, potentially greater savings could occur through more aggressive pricing policies for generics, see Table 1A. These though may take considerable time to implement; consequently, current practices in Germany could be a good compromise.

Demand-side measures to address physician and patient concerns have been successfully introduced in France leading to appreciable savings when combined with prescriptive pricing policies for generics, see Table 2. As a result, this provides direction to other countries faced with similar concerns. Similarly, the recent initiatives among MCOs in the US to enhance the use of generics within a class to improve both the quality and efficiency of care, especially where the outcome and safety of

**Table 1A: Price comparison of 50 leading generics and out of patent drugs with products reimbursed in Germany and UK (England and Wales)**

50 leading generic products in Germany	Active ingredients	Germany (DE)		United Kingdom (UK)		Potential savings
		Total sales without VAT (19%)	Total PRP sales without VAT (19%)	Total sales (Million GBP) <sup>1</sup>	Total sales in German pack size (Million Euros)	Million Euros
		Million Euros				
<b>Sifrol</b> 0.35 mg	Pramipexole	183.4 100 tablets	216.91 100 tablets	127.34 100 tablets	143.60 100 tablets	62.0
<b>Keppra</b> 1,000 mg	Levetiracetam	178.3 200 tablets	609.19 200 tablets	89.10 60 tablets	335.94 60 tablets	79.9
<b>Arimidex</b> 1 mg	Anastrozol	127.1 100 tablets	505.86 100 tablets	68.56 28 tablets	277.79 28 tablets	57.3
<b>Actrapid human</b> Penfill 100 I.E./mL	Human insulin	117.1	75.47	7.48	28.15	73.4
		10 × 3 mL patrons		5 × 3 mL patrons		
<b>Simvastatin-1A Pharma</b> 40 mg	Simvastatin	110.8 100 tablets	25.81 100 tablets	1.17 28 tablets	8.28 28 tablets	75.3
<b>Prograf</b> 1 mg	Tacrolimus	100.7 100 capsules	426.72 100 capsules	80.28 50 capsules	181.81 50 capsules	57.8
<b>Omepr</b> 20 mg	Omeprazole	100.0 100 tablets	36.16 100 tablets	1.62 28 tablets	10.08 28 tablets	72.1
<b>Plavix</b> 75 mg	Clopidogrel	94.7 100 tablets	233.26 100 tablets	35.64 30 tablets	136.39 30 tablets	39.3
<b>L-Thyroxin Henning</b> 100 µg	Levothyroxine	88.4 100 tablets	12.49 100 tablets	0.99 28 tablets	7.56 28 tablets	34.9
<b>Ibuprofen Lichtenstein</b> 600 mg	Ibuprofen	80.1 50 tablets	11.47 50 tablets	3.96 84 tablets	3.24 84 tablets	57.5
<b>Novaminsulfon-ratiopharm</b> 500 mg	Metamizole	78.5 50 tablets	11.07 50 tablets			0
<b>RamiLich</b> 5 mg	Ramipril	77.2 100 tablets	11.00 100 tablets	1.52 28 tablets	9.68 28 tablets	9.3
<b>CellCept</b> 500 mg	Mycophenolate	74.8 150 tablets	480.30 150 tablets	82.26 50 tablets	279.37 50 tablets	31.3
<b>Actraphane</b> 30 Flexpen 100 I.E./mL	Human insulin	74.4	81.10	28.32	65.44	14.4
		10 × 3 mL patrons		5 × 3 mL patrons		
<b>Temodal</b> 100 mg	Temozolamide	68.8 20 capsules	2,727.66 20 capsules	325.80 5 capsules	1,463.35 5 capsules	31.9
<b>MetoHEXAL</b> 95 mg	Metoprolol	65.5	14.49	3.56	8.92	25.2
		100 modified release tablets		56 tablets	56 tablets	
<b>Mono-Embolex</b> 3,000 I.E.	Certoparin	63.8	42.38			0
		10 prefilled syringes				
<b>Protaphane</b> Penfill 100 I.E./mL	Human insulin	61.3	75.47	17.50	41.21	27.8
		10 × 3 mL patrons		5 × 3 mL patrons		
<b>Singulair</b> 10 mg	Montelukast	56.7 100 tablets	175.56 100 tablets	26.97 28 tablets	111.46 28 tablets	20.7
<b>Insuman Rapid</b> 100 I.E./mL	Human insulin	54.6	75.47	17.50	41.21	24.8
		10 × 3 mL patrons		5 × 3 mL patrons		

(Continued)

**Table 1A: Price comparison of 50 leading generics and out of patent drugs with products reimbursed in Germany and UK (England and Wales) (Continued)**

50 leading generic products in Germany	Active ingredients	Germany (DE)		United Kingdom (UK)		Potential savings
		Total sales without VAT (19%)	Total PRP sales without VAT (19%)	Total sales (Million GBP) <sup>1</sup>	Total sales in German pack size (Million Euros)	Million Euros
		Million Euros				
<b>Omeprazol-ratiopharm</b> NT 20 mg	Omeprazole	54.1 100 tablets	36.15 100 tablets	1.62 28 tablets	10.08 28 tablets	39.0
<b>Arava</b> 20 mg	Leflunomid	50.8 100 tablets	412.12 100 tablets	61.36 30 tablets	232.40 30 tablets	22.1
<b>Salofalk</b> 500 mg	Mesalazin	50.0 300 tablets	128.83 300 tablets	24.21 100 tablets	84.35 100 tablets	17.3
<b>Pantoprazol Nyc</b> 40 mg	Pantoprazole	50.0 98 capsules	54.43 98 capsules	2.01 28 capsules	11.41 28 capsules	39.5
<b>SimvaHEXAL</b> 40 mg	Simvastatin	49.8 100 tablets	29.26 100 tablets	1.17 28 tablets	8.28 28 tablets	35.7
<b>Metformin axcount</b> 1,000 mg	Metformin	49.7 120 tablets	11.28 120 tablets	1.31 56 tablets	5.30 56 tablets	26.4
<b>Torasemid 1A Pharma</b> 10 mg	Torasemide	49.7 100 tablets	12.75 100 tablets	16.81 28 tablets	70.83 28 tablets	0.0
<b>Fentanyl HEXAL</b> 50 µg/h	Fentanyl	49.2	109.66 10 matrix patches	36.59 5 patches	83.96 5 patches	11.5
<b>Sandimmun Optoral</b> 50 mg	Ciclosporin	48.2 100 capsules	229.98 100 capsules	36.41 30 tablets	139.27 30 tablets	19.0
<b>RamiLich comp.</b> 5/25 mg	Ramipril + hydrochlorothiazide	47.6 100 tablets	19.37 100 tablets			0
<b>L-Thyrox HEXAL</b> 100 µg	Levothyroxine	45.7 100 tablets	13.46 100 tablets	0.99 28 tablets	7.56 28 tablets	20.0
<b>Iscover</b> 75 mg	Clopidogrel	45.7 100 tablets	223.57 100 tablets	35.64 30 tablets	136.39 30 tablets	17.8
<b>Oxygesic</b> 40 mg	Oxycodone	45.7	455.82 100 slow release tablets	99.77	201.30 56 slow release tablets	25.5
<b>Thyronajod</b> 75 µg	Levothyroxin + potassium iodine	45.0 100 tablets	18.42 100 tablets			0
<b>BisoLich</b> 5 mg	Bisoprolol	44.2 100 tablets	10.79 100 tablets	1.02 28 tablets	7.68 28 tablets	12.7
<b>Pentalong</b> 80 mg	Pentaerythryl-tetranitrate	43.1 100 tablets	30.02 100 tablets			0
<b>Trevilor</b> 75 mg	Venlafaxine	42.2	162.04 100 slow release capsules	22.08	45.95 56 slow release capsules	30.2
<b>Insuman Comb 25</b> 100 I.E./mL	Human insulin	41.6	75.47 10 × 3 mL patrons	17.50	41.21 5 × 3 mL patrons	18.9
<b>Diclo-1A Pharma</b> 75 mg	Diclofenac	41.3	8.78 20 slow release capsules	12.92	5.53 56 slow release capsules	15.3

(Continued)

**Table 1A: Price comparison of 50 leading generics and out of patent drugs with products reimbursed in Germany and UK (England and Wales) (Continued)**

50 leading generic products in Germany	Active ingredients	Germany (DE)		United Kingdom (UK)		Potential savings
		Total sales without VAT (19%)	Total PRP sales without VAT (19%)	Total sales (Million GBP) <sup>1</sup>	Total sales in German pack size (Million Euros)	Million Euros
		Million Euros				
<b>Clopidogrel HEXAL</b> 75 mg	Clopidogrel	39.9 100 tablets	124.69 100 tablets	2.50 30 tablets	12.69 30 tablets	35.9
<b>Pantoprazol HEXAL</b> 40 mg	Pantoprazole	39.2 100 tablets	41.66 100 tablets	2.01 28 tablets	11.64 28 tablets	28.2
<b>Amlodipin Dexcel</b> 5 mg	Amlodipine	38.6 100 tablets	9.25 100 tablets	0.93 28 tablets	7.32 28 tablets	8.1
<b>Euthyrox</b> 100 µg	Levothyroxine	38.2 100 tablets	12.46 100 tablets	0.99 28 tablets	7.56 28 tablets	15.0
<b>Pantozol</b> 40 mg	Pantoprazol	38.0 98 capsules	81.76 98 capsules	2.01 28 capsules	11.41 28 capsules	37.7
<b>Metex FS</b> 15 mg	Methotrexate	37.3	219.78	16.57	234.75	0
		12 injection vials		1 injection vial		
<b>Omeprazol KSK</b> 20 mg	Omeprazol	35.9 98 capsules	27.27 98 capsules	1.62 28 capsules	9.88 28 capsules	22.9
<b>Voltaren Resinat</b> 75 mg	Diclofenac	35.3	10.81	12.92	13.82	0
		50 slow release capsules		56 slow release capsules		
<b>Marcumar</b> 3 mg (D), <b>coumadine</b> 5 mg (UK)	Phenprocoumon	35.3 98 tablets	18.36 98 tablets	0.92 28 tablets	7.13 28 tablets	21.6
<b>Clopidogrel-ratiopharm</b> 75 mg	Clopidogrel	33.9 100 tablets	124.69 100 tablets	2.50 30 tablets	12.69 30 tablets	30.2
<b>Simvabeta</b> 40 mg	Simvastatin	31.9 100 tablets	27.85 100 tablets	1.17 28 tablets	8.28 28 tablets	22.4
Sum rank 1–50		3,153.9	8,588.62			1,371.4
Rank 1–50, share of total		27.4%				27.4%
Total generics market		11,504.2				5,005.1

The 50 leading products prescribed for sick fund outpatients in Germany in 2010 are shown with the total sales (Euros) for the indicated brand product in Germany without VAT (19%) (Column 3), the total pharmacy retail expenditure (PRP) for the 50 products without VAT (19%) (Column 4 – which includes the pharmacy mark-up based on the Gelbe Liste 6 June 2011 - www.gelbe-liste.de), pharmacy retail expenditure in the United Kingdom (UK) in British pounds (GBP) based on the Drug Tariff or British National Formulary (BNF) price for the pack (Column 5 - NHS Prescription Service: The June 2011 Electronic Drug Tariff 6 June 2011 - www.ppa.org.uk/ppa/edt\_intro.htm), and the price calculated for the corresponding German pack size in Euros (Column 6). The potential savings for the total sales of the product in Germany are calculated on basis of the British pharmacy retail prices (all prices per 6 June 2011) including allowances for pharmacy remuneration. <sup>1</sup>based on Drug Tariff or British National Formulary.

new drugs has not been established, also provides direction to other countries. This mirrors the situation in for instance Stockholm in Sweden with its ‘Wise List’ of approximately 200 recommended drugs in ambulatory care [64]. These are predominantly well-established generic drugs, with a recent ecological study showing no difference in surrogate measures in patients with diabetes, hypertension or hypercholesterolaemia between patients prescribed well-established generic drugs compared with those prescribed patent-protected drugs; however considerable differences in costs [65].

The combination of multiple supply- and demand-side measures has appreciably improved prescribing efficiency for high volume

drugs in Scotland, also providing direction to other countries, see Table 3. An important message, based on the experiences of NHS Bury, is for health authorities and health insurance agencies to pro-actively monitor products shortly losing their patent and plan for this through switching and other activities where this is possible, see Table 3. As a result, fully capitalise on generics as soon as they become available.

Additional measures to enhance the prescribing of generics include compulsory or voluntary INN prescribing. This has the potential to reduce patient confusion where patients are prescribed a different brand of generics at each prescription [9, 66] as well as the potential for duplication of

**Table 2: Selected successful country case histories principally dealing with demand-side measures to enhance the prescribing of generics****France [3, 4, 8, 51]**

## A) Recent measures in France to address patient and physician concerns with generics

## i) Physicians:

- French authorities (AFSSAPS) regularly publish and update the list of generic products available, with Health Insurance Funds providing continuous feedback to ambulatory care physicians on their generics prescribing rates benchmarked against local colleagues
- Voluntary Pay for Performance measure whereby approximately 40% of physicians eventually took part and received additional payment for increasing their prescribing of generics versus patented products in a class (ATC Level 4) or group of classes (ATC Level 3). Classes include antibiotics, proton pump inhibitors (PPIs), statins, antihypertensive drugs as well as antidepressants. Initially this was a pilot scheme, but has now been extended to all physicians in France

## ii) Pharmacists:

- Guaranteed the same absolute margin for both generic and originator medicines. They also receive a maximum discount of 17% of the ex-factory price for generic products
- Since 2006, substitution targets are determined annually and published as an amendment to the national agreement between the pharmacists and the Health Insurance Funds. The last amendment was published in April 2010 and, in addition to a list of molecules with specific targets, there was also a list of targets for each regional territory in France (approximately 100) to further enhance generics substitution

## iii) Patients:

- Government promotional campaigns to enhance the acceptance of generics and INN (international non-proprietary name) prescribing
- Health Insurance Funds promote generics on the back of reimbursement forms sent to patients
- Patients must pay the Health Insurance proportion of the cost of a drug if they refuse generics substitution, i.e. 30% for comfort drugs, 65% for the majority, and 100% for essential drugs (85% of the population have supplementary insurance covering the remainder where pertinent). However, they can claim this back from the Health Insurance but this takes time. If patients accept substitution, the pharmacists cover the cost of the Health Insurance proportion themselves and claim this back afterwards from the Health Insurance Fund

## B) Outcomes

The above measures, coupled with a prescriptive pricing policy for generics (prices 55% below the originator reducing by 7% after 18 months), led to annual savings estimated at Euros 1 billion in 2007, Euros 0.905 billion in 2008 and Euros 1.01 billion in 2009.

Additional measures are under consideration building on experiences across Europe.

**USA Managed Care Organizations (MCOs) – Blue Cross Blue Shield [9, 52-54]**

## A) Current situation

The prescribing of generics is a major priority area among MCOs in the US from both a cost saving as well as a clinical perspective.

Some manufacturers launch 'branded generics' at similar prices to originators. This is leading MCOs in recent years to closely monitor the situation and, in most cases, block these 'branded generics' from formulary inclusion. This is because the inclusion of branded generics may affect the overall level of rebates offered by pharmaceutical companies for reaching combined sales targets for all their originator products included in the formulary.

In addition, there is increasing awareness that the current situation of allowing six months exclusivity for the first generic drug on the market for a particular molecule also does not result in appreciable savings during this period. Consequently, again most MCO's now block the formulary inclusion of these generics especially if they reduce the level of rebates offered by the originator pharmaceutical company for the range of products on the formulary. Another option is to place these first generics on the third tier (typically MCOs have three to four Tiers on their formulary with successively higher co-payment from Tier One to Tier Four – mentioned earlier), which is associated with an appreciable higher patient co-payment. In addition, in some cases putting the originator in the generics tier (first tier for co-pay), and passing savings from moving the product from the second tier (higher co-payment) to the first tier directly onto members. The tier situation for both the originator and the generics is revised once multiple generics become available at appreciably lower acquisition prices than the first generic drug.

Alongside this, in the past generics utilisation has generally been promoted as 'cost saving', which has been perceived negatively by some members. This is resulting in MCOs now promoting generics under the 'clinical safety umbrella' alongside cost savings. The clinical evaluation conducted by many MCO Pharmacy and Therapeutic Committees now supports and broadcasts the utilisation of generics not only on the basis of cost savings once multiple sources are available but also on the basis of the clinical experience for a molecule. This arises from the long patent life, which provides considerable clinical and safety data including outcomes over time. These data are typically lacking from newly launched non-generic products.

*(Continued)*

**Table 2: Selected successful country case histories principally dealing with demand-side measures to enhance the prescribing of generics**

Regulatory support both by FDA and Centers for Medicare & Medicaid Services is contributing to the increased utilisation of generics. The economy is also a big driver of generics use, especially where employer groups are facing the challenges of increased costs due to the influx of premium priced me-too brands. Consequently, employers are now increasingly requesting formulary designs that will be cost-effective as well as clinically optimum, i.e. without compromising care. As a result, the introduction of Advantage formularies – where therapeutic classes that have generics available require a failure of a generic drug before a patent-protected product is prescribed – are becoming very popular, and almost every MCO is now offering this option.

The introduction of US\$4 generics programmes (Tier One) is also increasing the utilisation of generics, as well as increasing the awareness of generics among the general population. Many MCOs are also now actively promoting cross therapeutic opportunities for generics substitution where the effectiveness and safety of a particular generic product is similar to a patent-protected product in the same or related class, mirroring the situation in, for instance, Norway and the UK promoting substitution of patent-protected atorvastatin with generic simvastatin. This rationale for promoting this approach is enhanced when comparing the known efficacy and safety of generics versus newer patent-protected products with limited outcome and safety data. Consequently, it is likely that the steady increase in the percentage of prescriptions dispensed as generics will continue to rise beyond 78% of all prescriptions seen in 2010.

**B) Supreme Court Ruling and subsequent activities**

In the 2009 case *Wyeth vs Levine*, the Supreme Court in the US ruled that manufacturers of brand-name drugs could be sued under state law for failing to adequately warn patients of any new patient safety risks discovered after the drug was approved. The Supreme Court accepted though the FDA's beliefs of the situation regarding generics, and held that State Courts were preempted from making any finding of liability based on a generic drug manufacturer's failure to change its label. However, in the future, FDA believes that generics manufacturers have a duty to propose stronger warning labels if needed as more clinical data becomes available. This was a 5–4 decision, and a reversal of the previous rulings.

Alongside this, FDA is increasingly taking strict actions where they believe the safety of a generic drug is being breached, e.g. generic voltaren eye drops were withdrawn from the market when there were safety concerns.

As a result of this ruling, although still under discussion, it is likely the package insert of generics will be more regularly updated with safety information.

**Table 3: Selected successful country case histories principally dealing with both supply- and demand-side measures**

**Australia [55-57]**

**A) Measures and outcomes**

**i) First Initiatives**

A number of measures and initiatives have been introduced in Australia in recent years including:

- Brand Premium Policy where the Prescribing Benefits Scheme (PBS) subsidises the lowest priced brand of a medicine. Consumers have to pay extra for a more expensive molecule once multiple sources are available
- Brand Substitution Policy allows for a medicine to be dispensed as a generic medicine if agreed to by the patient

This breaks down as follows:

In 2007, the first wave of reforms of the PBS aimed to align government payments for medicines to pharmacy purchase prices for generic medicines. The measures included:

- Creation of two separate formularies: F1 consists of drugs where there is only one brand of a specific medicine listed on the PBS and F2 which consists of drugs with two or more brands including branded generics
- F2 is further broken down into F2A which contains all drugs that were not subject to high levels of discounting to pharmacies on 1 October 2006 and F2T which contains all drugs that were subject to high levels of discounting to pharmacies on 1 October 2006
- A series of statutory price reductions to medicines contained within F2 – 2% price reductions for F2A drugs in August 2008, August 2009 and August 2010, and a 25% price reduction for F2T drugs in August 2008
- An automatic 16% price reduction policy the first time a new branded generic drug is listed on the PBS
- Progressive introduction of a system of price disclosure for all F2 medicines from August 2007 for drugs listed on the F2A formulary and December 2010 for all other F2 medicines

**ii) Outcomes**

- The first assessment of the impact of the 2007 PBS reforms showed that the reduction in PBS outlays from the statutory price reductions was AUD 274 million in 2008–09
- This though was still lower than the total cost to government of structural adjustment package (AUD 359.3 million) mainly paid to community pharmacies and to wholesalers.

*(Continued)*

**Table 3: Selected successful country case histories principally dealing with both supply- and demand-side measures (Continued)**

B) Subsequent initiatives

- These results prompted a second wave of reforms in October 2010 that included further price reductions—these were a further 2% for drugs on the F2A formulary and 5% on F2T formulary in October 2010
- Alongside this, greater transparency in generics price disclosures that included a minimum weighted average price disclosure-related price reduction of 23% for those F2 drugs in the review cycle from December 2010 to April 2012

C) Proposed changes

Further initiatives to reduce generics prices are ongoing with improved knowledge of the level of rebates offered by generics manufacturers to community pharmacies to enhance their market share

D) Ongoing demand-side measures:

- i) Patients: Government promotional campaigns (TV, brochures in community pharmacies, and National Prescribing Service campaigns) to enhance the acceptance of generics among the population
- ii) Pharmacists: In the 5th Community Pharmacy Agreement there is a Premium Free Dispensing Incentive Payment. From 1 July 2010, a fee of AUD 1.53 is paid to community pharmacists for each substitutable brand dispensed where a Premium does not apply

**Lithuania [10, 12, 58-60]**

A) Measures

Measures introduced in Lithuania in 2009/2010 building on existing measures to reduce pharmaceutical expenditure following the financial crisis (mandated 8% reduction in 2010 versus 2009) whilst ensuring the availability of medicines included:

- The first generics of a molecule to receive marketing authorisation must be priced at least 30% below the originator to be reimbursed
- The second and third generics must be priced at least 10% below the first generics to be reimbursed
- Market forces after this to lower the prices of the fourth and subsequent generics with patients having to cover the additional costs themselves for a more expensive drug than the current referenced priced molecule (typically the lowest priced molecule)
- When more than three products with the same INN name are eligible to be reimbursed, the originator must not be priced higher than 50% above the average price of the two cheapest generics for continued reimbursement
- INN prescribing is mandatory unless a biological drug is prescribed or physicians receive prior approval from the Hospital or Polyclinic Therapeutic Committee (rules tightened June 2010 with concerns with abuse with the previous voluntary system)
- Pharmacists are obliged to stock the cheapest generics with financial penalties if they do not comply. Initially this is a fine of 100 LTL (Euros 30); with further abuse resulting in pharmacies no longer being able to dispense prescriptions on behalf of the National Health Insurance Fund of Lithuania

B) Outcome

- The above measures, coupled with obligatory price volume agreements for new innovative drugs that could increase the pharmaceutical budget, enabled the Health Insurance Fund to decrease pharmaceutical expenditure in 2010 whilst increasing the number of prescriptions by 9%
- Alongside this, the Health Insurance Fund has been able to obtain appreciable price reductions for a range of generic PPIs, statins and ACEIs in 2007 or 2009 versus 2000 or 2001 originator prices. These mirror those among a range of European countries demonstrating that it is possible for European countries with smaller populations to engineer low prices for their drugs despite the rhetoric
- As a result of the various initiatives, there was no reduction in accessibility to drugs in Lithuania in 2010 despite reduced pharmaceutical expenditure

**UK—England including Primary Care Trusts [4, 8, 9, 11, 21, 61]**

A) Supply-side measures – ‘M’ (manufacturer) and ‘W’ (wholesaler) scheme and outcome

- The introduction of the ‘M’ and ‘W’ scheme throughout the UK, with its increasing transparency in the pricing of generics, as well as discounts and rebates offered by manufacturers to community pharmacists to preferentially dispense their generics, led to an average 32.4% reduction in the prices of generics within the first year of introduction in 2005
- This resulted in a 2% reduction in overall pharmaceutical expenditure the year following its introduction
- Prior to this, there were higher tariff prices with generics manufacturers offering discounts of up to 80% or more to community pharmacists to preferentially dispense their particular generics. Following this scheme, reimbursed prices (tariff price), for example, for lower strength simvastatin have been as low as 2% of pre-patent loss originator prices

(Continued)

**Table 3: Selected successful country case histories principally dealing with both supply- and demand-side measures (Continued)**

B) Additional measures

- Following the instigation of the ‘M’ and ‘W’ scheme (above), there is usually active monitoring of Tariff prices by Pharmaceutical Advisers in the various Primary Care Trusts (PCTs) to enhance potential savings
- There is also active monitoring of drug patent expiry dates to help set future drug budgets for GPs, as well as enhance prescribing efficiency through identifying potential opportunities for switching prescriptions to therapeutically equivalent drugs in the same class ahead of generics availability, e.g. different statins and different angiotensin receptor blockers. As a result, help maximise early potential savings following new generics becoming available. The alternative is continual ‘catch-up’ post launch
- The setting of drug budgets using intelligence of likely patent losses has been ongoing in for instance NHS Bury for the past 5 years, with a high degree of accuracy—within 1% either side of estimations—to enhance prescribing efficiency

**UK—Scotland [4, 8, 9, 11, 21, 43]**

A) Demand-side measures

- Alongside the ‘M’ and ‘W’ scheme, Scotland has introduced multiple demand-side measures in recent years to help conserve resources whilst not compromising care
- Demand-side measures include medical education encouraging INN prescribing, academic detailing encouraging the prescribing of multiple sourced products first line, guidelines, prescribing decision support systems, monitoring and benchmarking of prescriptions, prescribing and quality targets including the percentage of generic PPIs versus all PPIs; generic statins versus all statins, and % ACEIs versus all renin-angiotensin inhibiting drugs, as well as financial incentives for GPs

B) Outcome

- Reimbursed expenditure/1,000 inhabitants for PPIs in 2010 was 56% below 2001 levels despite a 3-fold increase in utilisation from 2001 to 2010 (defined daily doses [DDD] basis), with expenditure/DDD for generic omeprazole in 2010 91% below 2001 originator prices
- Reimbursed expenditure for the statins up by only 7% in 2010 compared with 2001 despite a 6.2 fold increase in utilisation during this period (DDD basis), with expenditure/DDD for generic simvastatin in 2010 97% below 2002 originator prices
- Reimbursed expenditure on renin-angiotensin inhibiting drugs remaining similar between 2001 and 2007 despite a 159% increase in utilisation (DDD basis) during this period
- High INN prescribing rates – averaging over 83% across all products and 98% for generic omeprazole and generic simvastatin in 2010. It is expected that high INN prescribing rates help address potential patient confusion that may arise with different product names (through branded generics) once multiple sources become available

**Table 4: Country case histories where health authorities have failed to realise the full benefits from the availability of generics**

**Abu Dhabi [17, 62]**

A) Measures

Health Authority Abu Dhabi (HAAD) introduced a ‘unified prescription form’ (March 2009) mandating INN prescribing with minor exceptions. This combined with a comprehensive generic drug policy (August 2009) sought to increase generics utilisation in Abu Dhabi. However:

- Pharmacists were, and are still, fully reimbursed for dispensing any molecule and receive bonuses from manufacturers to preferentially dispense their product (originator or branded generics)
- Originator manufacturers did not, and still do not, have to lower their prices for reimbursement following generics availability, and patients did not, and still do not, pay the price difference for a more expensive molecule than the current lowest priced molecule
- Currently limited demand-side measures in place encouraging physicians to prescribe a generic drug versus patent protected products in a class, or related class, where seen as essentially similar in outcomes for all or nearly all patients

B) Outcomes

- In the top eight classes by reimbursed expenditure, including the PPIs and statins, the utilisation of patent-protected products actually increased following the availability of multiple sourced products in each class rather than decreased
- As a result, ambulatory care expenditure actually increased in five of the top eight drug expenditure classes by 34.4% to US\$59.21 million in the 12 months up to November 2009 versus 12 months to November 2008. This was despite the availability of generics in each class

(Continued)

**Table 4: Country case histories where health authorities have failed to realise the full benefits from the availability of generics (Continued)**

## C) Future measures

- As a result of these findings, HAAD is currently considering a number of policies building on successful initiatives among European and other countries to increase the prescribing of generics in a class
- These include educational activities, economic incentives, as well as the introduction of reference pricing for the molecule with reimbursement based on the lowest price generics. The introduction of these combined demand-side measures practices will be facilitated by the introduction of Pharmacy Benefit Management to monitor prescribing habits against agreed guidance
- The combination of these various measures were estimated to potentially reduce PPI expenditure in 2010 by AED (Arab Emirates Dirham) 32.8 million (Euros 6.26 million) and statin expenditure by over AED 27 million (Euros 5.15 million) in the 1.75 million population of Abu Dhabi. However, potential savings for the statins are now reduced with the recent availability of generic atorvastatin in Abu Dhabi.

**UK–Primary Care Trusts**

## A) Measures

- As part of their monitoring of Drug Tariff prices and drug utilisation (Table 3), NHS Bury uses existing prescribing decision support systems to provide price change information in their recommendations to GPs about which preparations to prescribe
- However, the manufacturers of some branded generics seek to undercut Drug Tariff prices
- Occasionally, these manufacturers are ‘caught short’ if the Tariff drops below current prices of branded generics
- As a result, the manufacturers of these branded generics typically reduce their prices to maintain their promise to the PCTs of providing lower cost alternatives to current generics
- However, branded generics are not ideal for the NHS as they reduce the discounts and rebates potentially available to community pharmacies. This shortfall has to be made up out of their other payments, which is not ideal
- Branded generics also reduce competition amongst generics suppliers. Consequently, branded generics are typically not recommended by PCTs in their prescribing support systems

## B) Outcomes

- It is difficult to state the outcome of these monitoring activities among PCTs in England. However, PCTs and community pharmacists need to be alert to the activities of manufacturers supplying branded generics to make sure that neither party loses out in the long term
- As a result, provide guidance to other countries and regions in similar circumstances

**US–State Medicaid Services [63]**

## A) Current measures

- State Medicaid programmes have implemented a number of policies in recent years to reduce the rising costs of medications including generics substitution
- However, these policies differ in the extent to which pharmacists or patients can influence the medications they choose. States that implemented policies requiring patients’ consent prior to generics substitution experienced rates of substitution 25% lower in 2006/2007 than those States that did not

## B) Outcomes and implications

- It was estimated in 2007 that if the States currently requiring patient consent proactively eliminated this, they could save more than US\$100 million annually in the coverage of three top-selling medications nearing patent expiration
- There would also be savings from existing multiple sourced drugs

prescriptions. In addition, reduce the need for pharmacists to spend time addressing possible confusion among patients with associated costs. These issues will be explored further in future issues of this journal.

Potential pitfalls to avoid, based on the experiences of the co-authors, include not fully addressing all key stakeholders when initiating reforms to encourage the prescribing and dispensing of generics as seen in Abu Dhabi, see Table 4. However, this is now being addressed. In addition, not allowing pharmacists to dispense the cheapest drug once multiple sources are available, which is typically a generic versus an originator drug, in all but a minority of situations that could compromise patient care. Alongside this, delaying the instigation of measures

to enhance INN prescribing, compulsory substitution, as well as other measures to enhance the prescribing of particular generics need to be discussed and agreed in advance of their availability, to enhance physician acceptance as seen in Abu Dhabi, Austria and Sweden [7, 14, 17, 49].

Other pitfalls to avoid include long delays between marketing authorisation and the reimbursement of a generic drug [19]. These issues are also currently being addressed to enable payers to take full financial advantage of the availability of generics. There have also been situations where generics companies have been able to launch new generics ahead of patent loss by launching them in different salts to those of the originator such as generic clopidogrel. This is outside the scope of this

paper, but has been explored elsewhere in this issue of the *GaBiJournal*.

As discussed, we accept there are limitations with the study design. However, we believe the selected case histories provide useful lessons to other countries regarding which measures could potentially further enhance their prescribing efficiency. The sharing of information about potential policies and measures is vital if Europe is to maintain the ideals of comprehensive and equitable health care. Similarly, in the US, given current financial concerns, there is a greater need than ever before for further measures to help stem the rise in pharmaceutical expenditure.

### Conclusion

Payers across countries have successfully introduced multiple supply- and demand-side measures to improve prescribing efficiency through increased use of generics versus originators and patent-protected products in the same or related classes as well as measures to obtain low prices for generics. As a result, they are increasingly able to take full advantage of the availability of generics.

However, this has not always been possible. It is important though that countries continually share their experiences, and even start to accelerate the sharing of lessons learned about which policies and new measures appear the most effective, as resource pressures grow. The alternative is insufficient funds to cover the costs of increased drug volumes or new innovative drugs, both of which are not in the best interests of all key stakeholder groups.

### For patients

Expenditure on pharmaceuticals is a growing concern among health authorities and health insurance agencies as it is now the largest or equalling the largest component of expenditure in ambulatory, i.e. non-hospital, care. In addition, utilisation and expenditure on pharmaceuticals will continue growing driven by a number of factors including ageing populations, and hence a growing prevalence of chronic diseases leading to greater use of drugs, as well as new drugs being launched that are typically more expensive than existing drugs.

Consequently, health authorities and health insurance agencies welcome the availability of generics as these are priced lower than the originators to help ease resource pressures especially in these difficult economic times. However, the extent of the prescribing and dispensing of generics versus originators, as well as similar patent protected drugs in the same class to treat the same patients, varies considerably among countries. This can be due to concerns with the effectiveness of generics versus originators. However, this has been found not to be the case in extensive studies, especially with the tests required by the authorities to demonstrate similar bioavailability between generics and originators before products are launched onto the market. There are also considerable differences in the prices of generics among countries.

Health authorities and health insurance agencies need to tackle both these issues to release considerable resources to help fund comprehensive and equitable health care particularly in Europe without prohibitive increases in either taxes or health insurance

premiums. Consequently, they need to learn from each other with respect to measures that have been successful in other countries to enhance the prescribing and dispensing of generics at increasingly lower prices, as well as the pitfalls to avoid. The case histories described in this paper help them to achieve this aim.

### Disclosure of financial and competing interests

All authors have been especially invited for their direct role in introducing policy initiatives with regard to generics in their regions or countries, drawn from relevant health authorities or health insurance companies and their advisers. All authors have taken full part in the compilation and production of this paper.

Mohammed Abuelkhair (Abu Dhabi), Agnes Vitry (Australia), Shajahan Abdu (Abu Dhabi), Marion Bennie (Scotland, UK), Iain Bishop (Scotland, UK), Sahar Fahmy (Abu Dhabi), Karuoliene Garuoliene (Lithuania), Harald Herholz (Germany), Saira Jan (USA), Andrew Martin (UK), Rickard Malmström (Sweden), Ulrich Schwabe (Germany), Catherine Sermet (France), Peter Skiöld (Sweden), Luka Vončina (Croatia), are employed directly by health authorities, physician associations (Germany) or health insurance agencies, or are advisers to these organisations.

No author has any other relevant affiliation or financial involvement with any organisation or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript.

No writing assistance from commercial organisations was utilised in the production of this manuscript.

This study was in part supported by grants from the Karolinska Institutet.

**Provenance and peer review:** Commissioned; externally peer reviewed.

### Authors

- <sup>1</sup> Institute for Pharmacological Research Mario Negri, 19 Via Giuseppe La Masa, IT-20156 Milan, Italy, godman@marionegri.it
- <sup>2</sup> Prescribing Research Group, University of Liverpool Management School, Chatham Street, Liverpool L69 7ZH, UK.
- <sup>3</sup> Department of Laboratory Medicine, Division of Clinical Pharmacology, Karolinska Institutet, Karolinska University Hospital Huddinge, SE-14186, Stockholm, Sweden, brian.godman@ki.se, lars-l.gustafsson@ki.se
- <sup>4</sup> Drugs and Medical Products Regulation, Health Authority Abu Dhabi (HAAD), PO Box 5674, Abu Dhabi, United Arab Emirates, abuelkhair@haad.ae, shajahan@haad.ae, sfahmy@haad.ae
- <sup>5</sup> Quality Use of Medicines and Pharmacy Research Centre, Sansom Institute, School of Pharmacy and Medical Sciences, University of South Australia, Adelaide SA 5001, Australia, agnes.vitry@unisa.edu.au
- <sup>6</sup> Strathclyde Institute for Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, UK, marion.bennie@strath.ac.uk

## REVIEW ARTICLE

- <sup>7</sup> Information Services Division, NHS National Services Scotland, 1 South Gyle Crescent, Edinburgh EH12 9EB, UK, m.bennie@nhs.net, iain.bishop@nhs.net
- <sup>8</sup> Medicines Reimbursement Department, National Health Insurance Fund, Europos a., LT-03505 Vilnius, Lithuania, kristina.garuoliene@vlk.lt
- <sup>9</sup> Kassenärztliche Vereinigung Hessen, 15 Georg Voigt Strasse, DE-60325 Frankfurt am Main, Germany, harald.herholz@kvhessen.de
- <sup>10</sup> NHS Bury, 21 Silver Street, Bury BL9 0EN, UK, andrew.martin8@nhs.net
- <sup>11</sup> Department of Medicine, Clinical Pharmacology Unit, Karolinska Institutet, Karolinska University Hospital Solna, SE-17176 Stockholm, Sweden, rickard.malmstrom@ki.se
- <sup>12</sup> Department of Pharmacy Practice and Administration, William Levine Hall, Rm 416, Ernest Mario School of Pharmacy, Rutgers, The State University of New Jersey, 160 Frelinghuysen Road, Piscataway, New Jersey, NJ 08854, USA
- <sup>13</sup> Horizon Blue Cross Blue Shield of New Jersey, New Jersey, USA, saira\_jan@horizon-bcbnsj.com
- <sup>14</sup> University of Heidelberg, Institute of Pharmacology, DE-69120 Heidelberg, Germany, ulrich.schwabe@pharma.uni-heidelberg.de
- <sup>15</sup> IRDES, 10 rue Vauvenargues, FR-75018 Paris, France, semet@irdes.fr
- <sup>16</sup> Dental and Pharmaceuticals Benefits Agency (TLV), PO Box 22520, 7 Flemingatan, SE-10422 Stockholm, Sweden, peter.skiold@tlv.se
- <sup>17</sup> Ministry of Health, Republic of Croatia, 200a Ksaver, HR-10000, Zagreb, Croatia, luka.voncina@miz.hr
- <sup>11.</sup> Vončina L, Strizrep T, Godman B, Bennie M, et al. Influence of demand side measures to enhance renin-angiotensin prescribing efficiency in Europe: implications for the future. *Expert Rev Pharmacoecon Outcomes Res.* 2011; 11(4):469-79.
- <sup>12.</sup> Garuoliene K, Alonderis T, Marcinkevičius M. Pharmaceutical policy and the effects of the economic crisis: Lithuania. *Eurohealth.* 2011;17:1-4.
- <sup>13.</sup> Voncina L, Strizrep T. Croatia: 2009/2010 pharmaceutical pricing and reimbursement forum. *Eurohealth.* 2011;16(4):20-2.
- <sup>14.</sup> Godman B, Bucsecs A, Burkhardt T, Haycox A, Seyfried H, Wieninger P. Insight into recent reforms and initiatives in Austria; implications for key stakeholders. *Expert Rev Pharmacoecon Outcomes Res.* 2008;8(4):357-71.
- <sup>15.</sup> Godman B, Schwabe U, Selke G, Wettermark B. Update of recent reforms in Germany to enhance the quality and efficiency of prescribing of proton pump inhibitors and lipid lowering drugs. *Pharmacoeconomics.* 2009;27(5): 435-8.
- <sup>16.</sup> Coma A, Zara C, Godman B, Augusti A, Diogene E, et al. Policies to enhance the efficiency of prescribing in the Spanish Catalan region: impact and future direction. *Expert Rev Pharmacoecon Outcomes Res.* 2009;9(6):569-81.
- <sup>17.</sup> Abuelkhair M, Abdu S, Godman B, et al. Imperative to consider multiple initiatives to maximize prescribing efficiency from generic availability: case history from Abu Dhabi. *Expert Rev Pharmacoecon Outcomes Res.* 2012;12(1):115-24.
- <sup>18.</sup> Godman B, Malmstrom RE, Bennie M, Sakshaug S, et al. Prescribing restrictions – a necessary strategy among some European countries to enhance future prescribing efficiency? *Reviews in Health Care.* 2012;3(1):5-16.
- <sup>19.</sup> Sheppard A. Generic Medicines: Essential contributors to the long-term health of society [homepage on the Internet]. [cited 2012 May 22]. Available from: [http://www.imshealth.com/imshealth/Global/Content/Document/Market\\_Measurement\\_TL/Generic\\_Medicines\\_GA.pdf](http://www.imshealth.com/imshealth/Global/Content/Document/Market_Measurement_TL/Generic_Medicines_GA.pdf)
- <sup>20.</sup> Simoens S. International comparison of generic medicine prices. *Curr Med Res Opin.* 2007;23:2647-54.
- <sup>21.</sup> Duerden M, Hughes D. Generic and therapeutic substitutions in the UK: are they a good thing? *Br J Clin Pharmacol.* 2010;70(3):335-41.
- <sup>22.</sup> Simoens, S. Trends in generic prescribing and dispensing in Europe. *Exp Rev Clin Pharmacol.* 2008;1(4):497-503.
- <sup>23.</sup> Baumgärtel C. Myths, questions, facts about generic drugs in the EU. *Generics and Biosimilars Initiative Journal (GaBi Journal).* 2012;1(1):34-8. doi: 10.5639/gabij.2012.0101.009
- <sup>24.</sup> Baumgärtel C, Godman B, Malmström RE, Andersen M, et al. What lessons can be learned from the launch of generic clopidogrel? *Generics and Biosimilars Initiative Journal (GaBi Journal).* 2012;1(2):58-68. doi: 10.5639/gabij.2012.0102.016
- <sup>25.</sup> Kesselheim A, Stedman M, Bubrick E, et al. Seizure outcomes following the use of generic vs. brand-name antiepileptic drugs. A systematic review and meta-analysis. *Drugs.* 2010;70(5):605-21.
- <sup>26.</sup> Kesselheim A, Misoni A, Lee J, et al. Clinical equivalence of generic and brand-name drugs used in cardiovascular disease – a systematic review and meta-analysis. *JAMA.* 2008;300:2514-26.
- <sup>27.</sup> Simoens S. A review of generic medicine pricing in Europe. *Generics and Biosimilars Initiative Journal (GaBi Journal).* 2012;1(1):8-12. doi: 10.5639/gabij.2012.0101.004
- <sup>28.</sup> CBI market survey - the pharmaceutical products market in the EU. Publication date: February 2010. Available from: [cbi.nl/?pag=85&doc=5152&typ=mid\\_document](http://cbi.nl/?pag=85&doc=5152&typ=mid_document)
- <sup>29.</sup> Shrank WH, Hoang T, Ettner S, et al. The Implications of Choice - Prescribing generic or preferred pharmaceuticals improves medication adherence for chronic conditions. *Arch Intern Med.* 2006;166:332-7.
- <sup>30.</sup> Shrank WH, Libermann JN, Fischer M, et al. The consequences of requesting 'dispense as written'. *Am J Med.* 2011;124:309-17.
- <sup>31.</sup> Heikkilä R, Mäntyselkä P, Hartikainen-Herranen K, Ahonen R. Customers' and physicians' opinions of experiences with generic substitution during the first year in Finland. *Health Policy.* 2007;82(3):366-74.

## References

1. Godman B, Wettermark B, Bishop I, Burkhardt T, et al. European payer initiatives to reduce prescribing costs through use of generics. *Generics and Biosimilars Initiative Journal (GaBi Journal).* 2012;1(1):22-7. doi: 10.5639/gabij.2012.0101.007
2. Cameron A, Ewen M, Ross-Degnan D, Ball D, Laing R. Medicine prices, availability and affordability in 36 developing and middle-income countries; a secondary analysis. *Lancet.* 2009;373(9659):240-9.
3. Semet C, Andrieu V, Godman B, et al. Ongoing pharmaceutical reforms in France; implications for key stakeholder groups. *Appl Health Econ Health Policy.* 2010;8:7-24.
4. Godman B, Shrank W, Wettermark B, Andersen M, et al. Use of generics – a critical cost containment measure for all healthcare professionals in Europe? *Pharmaceuticals.* 2010;3(8):2470-94. doi: 10.3390/ph/3082470 ISSN 1424-8247
5. Godman B, Shrank W, Andersen M, et al. Comparing policies to enhance prescribing efficiency in Europe through increasing generic utilization: changes seen and global implications. *Expert Rev Pharmacoecon Outcomes Res.* 2010;10(6):707-22.
6. Godman B, Burkhardt T, Bucsecs A, et al. Impact of recent reforms in Austria on utilization and expenditure of PPIs and lipid lowering drugs; implications for the future. *Expert Rev Pharmacoecon Outcomes Res.* 2009;9(5):475-84.
7. Godman B, Wettermark B, Hoffman M, et al. Multifaceted national and regional drug reforms and initiatives in ambulatory care in Sweden; global relevance. *Expert Rev Pharmacoecon Outcomes Res.* 2009;9(1):65-83.
8. Godman B, Shrank W, Andersen M, et al. Policies to enhance prescribing efficiency in Europe: findings and future implications. *Front Pharmacol.* 2011;1(141):1-16. doi: 10.3389/fphar.2010.00141
9. McGinn D, Godman B, Lonsdale J, et al. Initiatives to enhance the quality and efficiency of statin and PPI prescribing in the UK: impact and implications. *Expert Rev Pharmacoecon Outcomes Res.* 2010;10(1):73-85.
10. Garuoliene K, Godman B, Gulbinovič J, et al. European countries with small populations can obtain low prices for drugs: Lithuania as a case history. *Expert Rev Pharmacoecon Outcomes Res.* 2011;11(3):343-9.

32. Figueiras M, Alves N, Marcelino D, Cortes M, et al. Assessing lay beliefs about generic medicines: development of the generic medicines scale. *Psychol Health Med*. 2009;14(3):311-21.
33. Simoens S. Interchangeability of off-patent medicines: a pharmacoeconomic perspective. *Expert Rev Pharmacoecon Outcomes Res*. 2008;8(6):519-21.
34. Shrank W, Cox E, Fischer M, et al. Patients' perception of generic medications. *Health Affairs*. 2009;28:546-56.
35. Shrank W, Cadarette S, Cox E, Fischer M, Metha J, et al. Is there a relationship between patient beliefs or communication about generic drugs and medication utilization? *Med Care*. 2009;47(3):319-25.
36. Kjoenniksen I, Lindbaek M, Grannas A. Patients' attitudes towards and experiences of generic drug substitution in Norway. *Pharm World Sci*. 2006;28(5):284-9.
37. Hakonsen H, Toverud EL. A review of patient perspectives on generics substitution: what are the challenges for optimal drug use. *Generics and Biosimilars Initiative Journal (GaBI Journal)*. 2012;1(1):28-32. doi: 10.5639/gabij.2012.0101.008
38. European Commission [homepage on the Internet]. Communication from the Commission – Executive Summary of the Pharmaceutical Sector Inquiry Report. Reference EU Commission report. 8 July 2009 [cited 2012 May 22]. Available from: [http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/communication\\_en.pdf](http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/communication_en.pdf)
39. Andersson K, Sonesson C, Petzold M, et al. What are the obstacles to generic substitution? An assessment of the behaviour of prescribers, patients and pharmacies during the first year of generic substitution in Sweden. *Pharmacoepidemiol Drug Saf*. 2005;14:341-8.
40. Tsiantou V, Zavras D, Kousoulakou H, et al. Generic medicines: Greek physicians' perceptions and prescribing policies. *J Clin Pharm Ther*. 2009;34(5):547-54.
41. Morel C, McGuire A, Mossialos E. The level of income appears to have no consistent bearing on pharmaceutical prices across countries. *Health Affairs*. 2011;30(8):1545-52.
42. Matthew Goodman. A spoonful of sugar [homepage on the Internet]. *Sunday Times*; 27 Nov 2011 [cited 2012 May 22]. Available from: <http://alsumidaieim.blogspot.co.uk/2011/12/spoonful-of-sugar-by-matthew-by-matthew.html>
43. Bennie M, Godman B, Bishop I, Campbell S. Multiple initiatives continue to enhance the prescribing efficiency for the proton pump inhibitors and statins in Scotland. *Expert Rev Pharmacoecon Outcomes Res*. 2012;12:125-30.
44. World Health Organization (WHO) Guidelines for ATC classification and DDD assignment 2009. Oslo: WHO Collaborating Centre for Drug Statistics Methodology. [cited 2012 May 22]. Available from: [www.whocc.no](http://www.whocc.no)
45. World Health Organization [homepage on the Internet]. Introduction to Drug Utilisation Research. WHO International Working Group for Drug Statistics Methodology, WHO Collaborating Centre for Drug Statistics Methodology, WHO Collaborating Centre for Drug Utilization Research and Clinical Pharmacological Services. ISBN 92 4 156234 X (NLM classification: WB 330). [cited 2012 May 22]. Available from: [http://www.who.int/medicines/areas/quality\\_safety/safety\\_efficacy/Drug%20utilization%20research.pdf](http://www.who.int/medicines/areas/quality_safety/safety_efficacy/Drug%20utilization%20research.pdf)
46. Godman B, Haycox A, Schwabe U, et al. Having your cake and eating it: Office of Fair Trading proposal for funding new drugs to benefit patients and innovative companies. *Pharmacoeconomics*. 2008;26(2):91-8.
47. AOK-Rabattverträge bleiben auf Erfolgskurs [homepage on the Internet]. [cited 2012 May 22]. Available from: [http://www.aok-bv.de/presse/pressemitteilungen/2011/index\\_06121.html](http://www.aok-bv.de/presse/pressemitteilungen/2011/index_06121.html)
48. Schwabe U. Arzneiverordnungs 2010 im Überblick. In: Schwabe U, Paffrath D. *Arzneiverordnungs Report 2011*. Berlin, Heidelberg: Springer-Verlag GmBH; 2011. pp. 3-42.
49. Godman B. Implementing an effective generics policy - what can countries learn from each other. Austrian Ministry of Health 2011 [homepage on the Internet]. [cited 2012 May 22]. Available from: [http://www.basg.at/uploads/media/110322\\_Generics\\_Godmann.pdf](http://www.basg.at/uploads/media/110322_Generics_Godmann.pdf)
50. Wettermark B, Godman B, Andersson K, et al. Recent national and regional drug reforms in Sweden: implications for pharmaceutical companies in Europe. *Pharmacoeconomics*. 2008;26(7):537-50.
51. La maîtrise des dépenses de Médicaments 2010. Available via URL: [http://www.ccomptes.fr/fr/CC/documents/RELFSS/Rapport\\_securite\\_sociale\\_2011\\_maitrise\\_depenses\\_medicaments\\_4.pdf](http://www.ccomptes.fr/fr/CC/documents/RELFSS/Rapport_securite_sociale_2011_maitrise_depenses_medicaments_4.pdf) [Accessed 22 May 2012].
52. Glantz L, Annas G. Impossible? Outlawing state safety laws for generic drugs. *N Engl J Med*. 2011;365(8):681-3.
53. Stohr G. Generic-Drug Makers Shielded From Lawsuits, Top Court Says. April 2011 [cited 2012 May 22]. Available from: <http://www.bloomberg.com/news/2011-06-23/generic-drug-makers-shielded-from-lawsuits-top-court-says-1.html>
54. Godman B, Sakshaug S, Berg C, Wettermark B, Haycox A. Combination of prescribing restrictions and policies to engineer low prices to reduce reimbursement costs. *Expert Rev Pharmacoecon Outcomes Res*. 2011;11:121-9.
55. Australian Government, Department of Health and Ageing [homepage on the Internet]. The impact of PBS reform. Commonwealth of Australia 2010. [cited 2012 May 22]. Available from: [http://www.health.gov.au/internet/main/publishing.nsf/Content/95DCCB478B78DBD9CA2576C500130B0A/\\$File/Impact%20of%20PBS%20Reform%20Report.pdf](http://www.health.gov.au/internet/main/publishing.nsf/Content/95DCCB478B78DBD9CA2576C500130B0A/$File/Impact%20of%20PBS%20Reform%20Report.pdf)
56. Australian Government and Medicines Australia [homepage on the Internet]. Memorandum of understanding. May 2010. [cited 2012 May 22]. Available from: [http://www.health.gov.au/internet/main/publishing.nsf/Content/57EA4D44B1CFDA51CA257721000D1449/\\$File/MOU%20MA.pdf](http://www.health.gov.au/internet/main/publishing.nsf/Content/57EA4D44B1CFDA51CA257721000D1449/$File/MOU%20MA.pdf)
57. NPS Medicine Wise [homepage on the Internet]. New generics campaign to focus on safety around medicine brand choices. April 2011. [cited 2012 May 22]. Available from: [http://www.nps.org.au/\\_\\_data/assets/pdf\\_file/0005/123656/generics\\_media\\_release\\_trade\\_2011\\_04\\_01.pdf](http://www.nps.org.au/__data/assets/pdf_file/0005/123656/generics_media_release_trade_2011_04_01.pdf)
58. Godman B, Wettermark B, Bennie M, Burkhardt T, Garuoliene K, et al. Enhancing prescribing efficiency through increased utilisation of generics at low price. (E)Hospital. 2011;13;3:28-31.
59. Dylst P, Simoens S. Does the market share of generic medicines influence the price level? A European analysis. *Pharmacoeconomics*. 2011 Oct;29(10):875-82. doi: 10.2165/11585970-000000000-00000
60. McKee M, Stuckler D, Martin-Moreno J. Protecting health in hard times. *BMJ*. 2010;341:681-2.
61. Moon J, Flett A, Godman B, et al. Getting better value from the NHS drug budget. *BMJ*. 2011;342:30-2.
62. Abuelkhair M, Fahmy S, Godman B, Abdu S, Gustafsson LL. Cross national comparative drug utilisation studies demonstrate potential efficiency gains in Abu Dhabi. *Pharmacoepidemiol Drug Saf*. 2011;20:S96.
63. Shrank W, Choudhry N, Agnew-Blais J, Federman A, et al. State generic substitution laws can lower drug outlays under Medicaid. *Health Aff (Millwood)*. 2010;29:1383-90.
64. Gustafsson LL, Wettermark B, Godman B, Andersén-Karlsson E, Bergman U, et al. The 'Wise List' - a comprehensive concept to select, communicate and achieve adherence to recommendations of essential drugs in ambulatory care in Stockholm. *Basic Clin Pharmacol Toxicol*. 2011;108(4):224-33.
65. Norman C, Zarrinkoub R, Hasselström J, Godman B, Granath F, Wettermark B. Potential savings without compromising the quality of care. *Int J Clin Pract*. 2009;63(9):1320-6.
66. Frisk P, Rydberg T, Carlsten A, Ekedahl A. Patients' experiences with generic substitution: a Swedish pharmacy survey. *JPHSR*. 2011;2(1):9-15.