

# Initiatives in South Africa to enhance the prescribing of generic proton pump inhibitors: findings and implications

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**Background:** There have been multiple reforms in South Africa to conserve resources including policies to enhance generic use, such as compulsory generic substitution and copayments. However, there are concerns with the limited knowledge of their impact. **Objective:** The objective was to determine utilization and expenditure of different proton pump inhibitors (PPIs). **Methodology:** A retrospective drug utilization study was conducted on a prescription database of a medical aid administrator in 2010. **Results:** The limited prescribing of single-sourced PPIs accounted for 21.5% of total prescriptions. The limited use of originators omeprazole and lansoprazole accounted for 1.8 and 1.4% of total prescriptions for the molecule, respectively. Generic prices accounted for 36–68% of the originator in 2010. Patients received on average 2.91 PPI prescriptions during the year. **Conclusion:** Policies to enhance prescribing of generics appear working. Opportunities exist to further lower generic prices given low prices in some European countries.

**Keywords:** drug utilization • Europe • generics • PPIs • prices • South Africa

## Background

Medicines have made an appreciable contribution to improving health outcomes in recent years [1,2]. However, pharmaceutical expenditure is coming under increasing scrutiny worldwide [3,4], rising by more than 50% in real terms during the past decade among OECD countries [5]. As a result, expenditure on pharmaceuticals is now the largest, or equaling the largest, cost component in ambulatory care, and in some countries is up to 60% of total healthcare expenditure [3,4,6]. In addition in low- and middle-income countries, healthcare expenditure accounts for between 13 and 32% of total household expenditures with one in four poor households in low-income countries incurring potentially catastrophic healthcare expenses when family members become ill [7]. Typically, between 40 and 60% of households spend 100% of healthcare expenditure on medicines [7]. The goal in all countries including Europe is to provide sustained universal access to healthcare including medicines [8–13].

Different reforms and initiatives have been instigated across countries to conserve resources to fund new valued medicines as well as increased medicine volumes without increasing taxes, health insurance or out-of-pocket expenditures. This also includes increasing patient access to medicines where this is a concern.

Reforms and initiatives for established medicines include measures to increase the prescribing and dispensing of low-cost generics versus originators. Measures include encouraging International Nonproprietary Name (INN) prescribing through multiple initiatives, for example, UK; alternatively, instigating compulsory INN prescribing apart from a limited number of cases as seen in Lithuania [4,14,15]; alternatively, compulsory generic substitution and/or making patients pay the difference in price between a generic and a more expensive originator in addition to any copayment for the medicine dispensed [4,16–19]. Other measures include enhancing the prescribing of multiple-sourced

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(generic) medicines versus single-sourced medicines in a class where all the medicines in the class are seen as essentially therapeutically similar [4,20]; as a result, conserve resources without compromising care [4,20–23]. Pertinent classes include the proton pump inhibitors (PPIs), statins and the renin-angiotensin inhibitor drugs, which include both the angiotensin converting enzyme inhibitors and angiotensin receptor blockers [21,23–30]. Savings can be substantial with prices of generics as low as 2–10% of prepatent loss prices in some countries [15,17,24,31]. For instance, reimbursed expenditure for the PPIs and statins in The Netherlands fell by 58 and 14% respectively in 2010 versus 2000 despite a threefold and 3.8-fold increase respectively in utilization. This was helped by multiple demand-side measures increasing the utilization of generic PPIs at 2% of their prepatent loss prices [24]. In Scotland, multiple demand-side measures resulted in reimbursed expenditure for the PPIs in 2010 56% below 2001 levels despite a threefold increase in utilization [15].

South Africa is no different with generic prescribing and generic substitution targeted as possible mechanisms for cost containment. South Africa implemented mandatory generic substitution in May 2003, making it a legal requirement according to the Medicines and Related Substances Act (Act 101 of 1965) [32] to inform patients of the availability of alternative generic medicines to allow them to make an informed choice. Alongside this, many medical aid schemes in South Africa, including the database used in this study, will only reimburse the cost of the generic product, and a copayment is required if patients want the more expensive originator product. Generic prescribing accounted for almost 50% of the market in volume and for one-third of sales value [33] in 2005, up from 30% of the market in volume and 20% of sales value in 2004 [34]. However, little is known about the current situation including the prices of generics versus originators in the various classes. We would though expect to see increased utilization of generics in South Africa as more standard treatments become available as generics, especially with the introduction of mandatory generic substitution [35,36].

In South Africa, patients can also register certain chronic conditions with their medical insurance scheme and, if approved, can receive their medication under the chronic plan of the medical aid scheme. This option prevents the medical aid benefits of patients being depleted due to the often high cost and monthly prescriptions for chronic conditions. A chronic condition is defined as a condition for which treatment lasts for a period of at least three months. The Council for Medical Schemes in South Africa publishes a Chronic Disease List (CDL), which specifies the medication and

treatment for the 25 chronic conditions that are compulsory for pharmaceutical benefit managers (PBMs) to cover [37]. Although PPIs are not explicitly included, patients can apply for their condition to be registered as chronic at the discretion of the specific medical aid scheme that they belong to and this could include the prescribing of PPIs.

PPIs are one of the most frequently prescribed classes of medicines worldwide due to their effectiveness and limited side effects across a range of upper gastrointestinal disorders [38–40]. However, there are growing concerns with the overprescribing of PPIs across countries [38]. There are also concerns with the side effects of long-term use, that is an increase in infection rates including hospital and community-acquired pneumonia as well as osteoporosis, which can result in increased fracture rates [41–45]. Other authors though have not seen this association [46].

The primary aim of this study is to investigate the utilization of the different PPIs, including both multiple-sourced (generic) and patented (originator) PPIs, and their associated costs in South Africa to provide future guidance. The typical number of prescriptions prescribed in a year will also be investigated given the increasing safety concerns with long-term chronic use of PPIs.

## Methodology

A retrospective drug utilization study was conducted on a prescription database of a private medical aid administrator in South Africa. The healthcare system in South Africa consists of a public sector and a private sector. Healthcare in the public sector is provided by the national government for patients who are unable to afford a private medical aid, which currently accounts for over 89% of the population [47]. The private sector is funded by the income from patients, with people belong to one of the available private medical aid (insurance) schemes. These medical insurance schemes have electronic databases enabling accurate research to be conducted, with most medical insurance schemes administered by an administrator overseeing several individual medical aid schemes. This compares to the public sector where there is limited access to utilization and expenditure data, and available data are not routinely collected electronically [48]. Patient dosing data are also not accurately recorded electronically in the public system.

The database used in this study is from one of the administrators in South Africa and is considered representative of prescribing in the private healthcare sector since it includes patients from all the different provinces.

Data from the prescription database covered the year 2010 and included all medications prescribed, procedures and devices (a total of 2,126,264 records). Each medication record contained information on the

age and gender of the patient, with a unique number to identify each patient, the date of the prescription, detailed information on the dispensed drug (name, package size, formulation, strength and quantity), price and various reimbursement variables. As mentioned, only generic prices are reimbursed with patients covering the additional costs themselves if they wish a more expensive originator. The database contains details of the reimbursed costs as well as copayment details. Sales of over the counter (OTC) PPIs that are not reimbursed by the medical insurance schemes are not included in the database. However, details of OTC products are included if the cost of OTC products are included in individual medical aid insurance schemes. This is similar to the situation in Europe where typically expenditure on OTC medicines are not reimbursed; consequently, not included in health authority databases [20].

The Anatomical Therapeutic Chemical Classification System [49], Monthly Index of Medical Specialities [50] and the South African Medicines Formulary [51] were used to identify the medicines that were prescribed. For the purpose of this study, medicine items (prescriptions) were principally extracted and analyzed (Monthly Index of Medical Specialities category 12.4.4) as this contains all formulations [50]. A subanalysis was also performed on cost/defined daily dose (DDD) [49] for the various oral formulations, excluding intravenous and infusion powder formulations, to compare price differences between oral generic and originator PPIs in 2010. This would also enable comparisons with the price differentials seen between originator and generic PPIs among European countries to provide suggestions for the future if pertinent. This builds on comments in the background section.

Microsoft Access® and Excel® were used to analyze the data. Basic descriptive statistics were calculated. One Euro (€1.00) was equal to ZAR9.38 (South African Rand), one US Dollar (\$1.00) was equal to ZAR7.64 and one British Pound (£1.00) was equal to ZAR11.48 at the time of the study (30 June 2010).

## Results

A total of 20,537 PPIs were prescribed to 7060 patients over the year at a total cost of ZAR3,985,845.45 including any patient copayments. Patients received on average 2.91 (SD = 3.03) PPI prescriptions during the year (range: 1–28 prescriptions). The average age of patients was 44.10 (SD = 16.31) years (range: 0–96 years). Half of the patients (50.88%) were female. Only 18.6% of the prescriptions were claimed on the chronic option of the different medical aid schemes. Approximately 70% of PPI prescriptions (69.1%) were dispensed in quantities of 28 or 30 dosage units (tab-

lets or capsules) per month, or multiples thereof. A further 9.8% of prescriptions were dispensed in doses of 7, 14 or 15 units per month, with different units for the remainder. Typically in South Africa, repeat prescriptions are only dispensed for a period of one month. Consequently, if a patient receives a repeat for three months, the patient will have to come into the pharmacy three times to collect their supply for that specific month. This will reflect as three different prescriptions for the same patient in the study.

## Prescribing of PPIs

All five PPIs were available in South Africa in 2010. Omeprazole was the most prescribed PPI (Table 1), accounting for half of all PPIs prescribed (50.8%), followed by esomeprazole (19.8%) and lansoprazole (18%). Overall, single-sourced PPIs accounted for 21.5% of total PPIs in 2010 (Table 1).

Patients received on average 1.21 (SD = 0.49) different PPI active ingredients over the year from the average of 2.91 PPI prescriptions per year. Most patients (82%) were only prescribed one PPI active ingredient during the year, 15% two different PPI active ingredients, 2.75% three and 0.25% four different active ingredients.

Eight different trade names (brand names) of omeprazole were prescribed with one generic product (Altosec®; AspenPharmacare) accounting for 56% of all omeprazole prescriptions (Supplementary Table 1; www.futuremedicine.com/doi/suppl/10.2217/cer.14.70). The originator product (Losec®; AstraZeneca) accounted for 1.8% of total omeprazole prescriptions. Nine trade names of lansoprazole were prescribed, with the originator accounting for 1.4% of prescribing frequency (Supplementary Table 1). There were similar low prescribing rates for oral originators omeprazole and lansoprazole when prescriptions were converted into DDDs at 0.9 and 0.8% respectively (Supplementary Table 2). There were higher rates for originator pantoprazole at 16.7%.

Table 1. Prescribing frequency (items prescribed) of the proton pump inhibitors by gender in 2010.

Active ingredients	Number of prescriptions		Genders combined	
	Female	Male	n	%
Esomeprazole <sup>†</sup>	19.3	20.4	4073	19.8
Lansoprazole	17.4	18.7	3705	18.0
Omeprazole	51.4	50.1	10,429	50.8
Pantoprazole	10.3	9	1988	9.7
Rabeprazole <sup>†</sup>	1.6	1.8	342	1.7
Total	100	100	20,537	100

<sup>†</sup>Single-sourced medicines, that is, no generics available.

The average cost/prescription for lansoprazole and omeprazole, which were principally the generic versions, was ZAR154.42 and ZAR157.76 respectively versus ZAR308.97 for esomeprazole (Figure 1).

The high frequency of prescribing generic versus originator lansoprazole and generic versus originator omeprazole (98–99% by prescription and DDD) at lower costs (Table 2) resulted in lower costs versus frequency of prescribing for these two active ingredients compared with patented (single-sourced) esomeprazole (Figure 2).

Figure 3 shows a comparison of the average cost of the different named products (originator and branded generics) prescribed for lansoprazole, omeprazole and pantoprazole. For all three PPIs, the originator products were more expensive than the average cost of the different branded generics.

### Discussion

There are a number of different implications and conclusions that can be drawn from these results.

First, the policies including mandatory generic substitution to enhance the prescribing of generic versus originator PPIs appear to be working well in South Africa with the utilization of generic omeprazole and lansoprazole at 98–99% of total utilization for their respective molecules (DDD basis). There were similar findings with the statins with high utilization of generic statins versus originators in South Africa in recent years [52]. These results mirror the very high rates of utilization of generic versus originator omeprazole in The Netherlands (94% of total omeprazole on a DDD basis) and the UK (98% on a DDD basis) [15,24]. This was achieved in both countries through multiple demand-side measures including preferential pricing policies with financial incentives (The Netherlands) and encouraging INN prescribing (UK) [15,24]. However, we accept that further studies are needed before

definitive statements can be made about the extent of generic utilization in recent years in South Africa.

Policies to encourage the prescribing of lower cost generic versus single-sourced PPIs also appear to be working in South Africa with low utilization of esomeprazole (19.8% of total prescriptions) versus omeprazole, lansoprazole and pantoprazole combined (78.5%; Table 1). Similar high rates of prescribing of generic PPIs versus esomeprazole were seen in England, Germany, Scotland and Sweden, for example, esomeprazole was only 14% of total PPIs in Sweden in 2007 (DDD basis), 13% in Germany, 6.8% in Scotland in 2007 (6.3% in 2010) and 5.9% in England in 2007 with their multiple demand-side measures including reference pricing in a class, for example, Germany, to encourage the prescribing of low-cost PPIs [15,20]. This compares with 23% in France, 31% in Ireland and 46% in Norway in 2007 with few demand-side measures to counteract the influence of pharmaceutical companies [20]. However, there is the potential to lower the utilization of single-sourced PPIs in South Africa to further conserve resources based on the situation in the UK.

These figures suggest that there appears to be no problems with branded generic PPIs in South Africa. This mirrors the situation in Europe [4,15,17,24]. However, we acknowledge that we cannot say this with complete confidence as we have not undertaken specific studies comparing the outcomes of different branded generic PPIs with the respective originators in South Africa. However, our findings suggest that there should be no problems in routine clinical practice.

The chronic prescribing of PPIs does not appear currently to be an issue in South Africa with an average of 2.91 prescriptions per patient (typically 14 or 28 days – Supplementary Table 1) during the year. Again though, we cannot say this with certainty without looking at individual patients and individual PPIs. This will be the

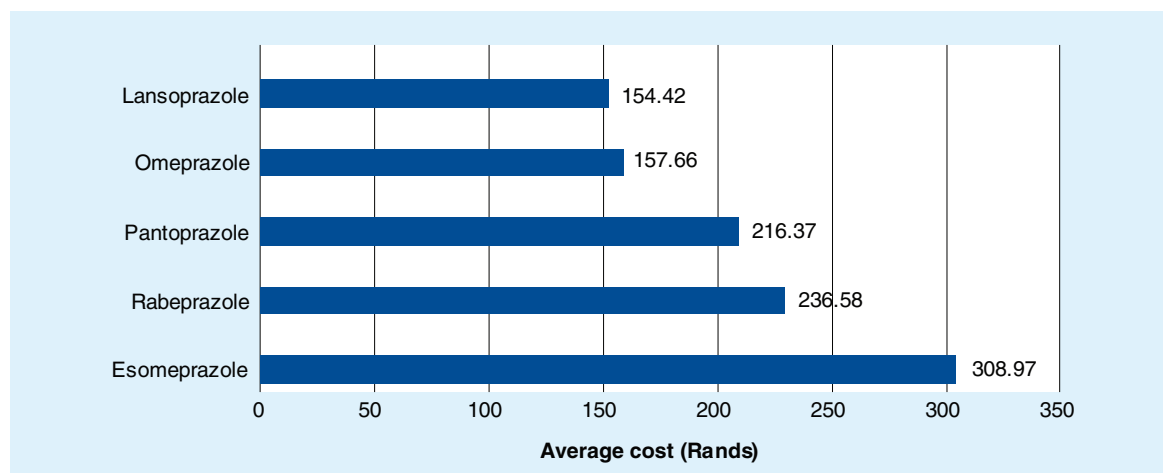


Figure 1. Average cost/prescription for each proton pump inhibitor in 2010 (South African Rand – ZAR).

subject of further research given the increasing patient safety concerns with chronic prescribing of PPIs discussed earlier.

However, there appears currently to be relatively high prices for generic PPIs in South Africa, that is, between 68 and 36% of the originator price which corresponds to a 32–64% price reduction on a cost/DDD basis (Table 2). Lower prices though were seen for some generic PPIs, for example, Nozer with a 79% price reduction (Supplementary Table 2). This compares with appreciably lower prices in The Netherlands, Scotland and Sweden where generic PPIs can be as low as 2–10% of prepatent loss prices, that is, 90–98% price reduction, despite strict bioequivalence criteria [15,17,24]. In addition, population size does not appear to be a barrier to obtaining low prices for generics as seen in Lithuania and the Republic of Srpska [14,53]. One possible reason for the high prices for generics in South Africa could be that they are ‘branded generics’ compared for instance with high INN prescribing rates in the UK [15]. However, this cannot be the only explanation as there are ‘branded generics’ in Sweden [17,54].

Potential ways forward for South Africa to achieve lower prices for generics could include either instigating a prescriptive pricing policy for generics as seen in Austria (60% below prepatent loss prices by the time the third generic is launched), France (55% below initially) or Norway (maximum of 85% below prepatent loss prices for high-volume generics), or alternatively instigating aggressive market forces [54]. Aggressive market forces could include increased transparency in the pricing of generics as seen in the UK with high INN prescribing rates coupled with regular requests for companies to provide data on the cost of producing generics as well as any rebates or discounts given to wholesalers or pharmacists to preferentially dispense a particular generic [15]; alternatively, instigating tendering systems as seen in The

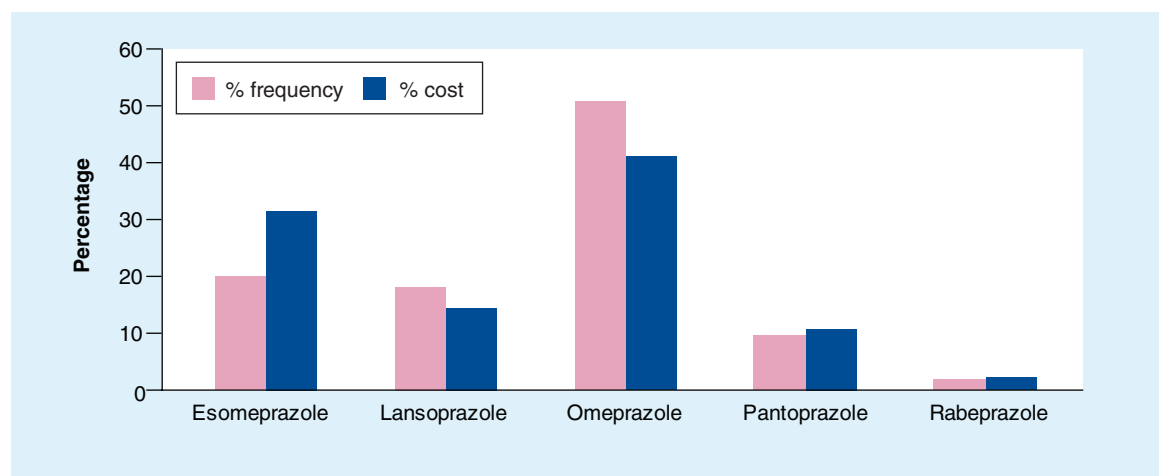
**Table 2. Cost (Rand)/defined daily dose for different oral proton pump inhibitors where generic versions exist.**

PPI	Cost/DDD	% of originator	% reduction
<b>Lansoprazole</b>			
Originator	16.95		
Total generics	6.14	36.3	63.7
<b>Omeprazole</b>			
Originator	13.26		
Total generics	5.43	41.0	59.0
<b>Pantoprazole</b>			
Originator	13.86		
Total generics	8.91	67.6	32.4

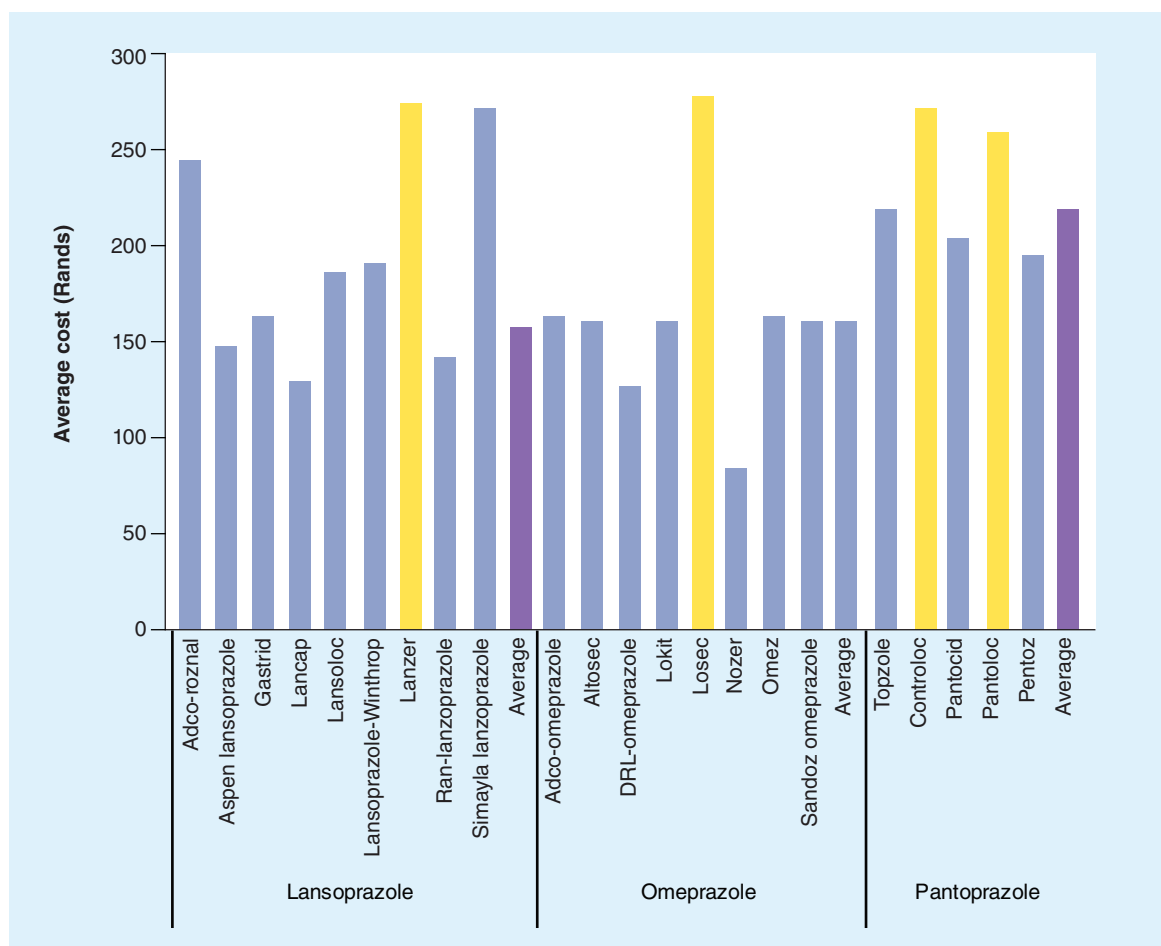
Controloc® (Nycomed) and Pantoloc® (Nycomed) have both been included as originator products for pantoprazole.  
DDD: Defined daily dose; PPI: Proton pump inhibitor.

Netherlands and Sweden [24,54]. In Sweden, there are now monthly auctions whereby the manufacturer that wins the bid for their particular generic is guaranteed an appreciable percentage of prescriptions the following month [54]. These are considerations for the future as the healthcare market in South Africa evolves.

There can also potentially be patient confusion if different branded generics each with different names are dispensed each time, especially with the wide variety of branded generic names currently available in South Africa (Supplementary Table 1). This happens in Sweden [17,54] if patients do not receive adequate information about their medicines [17,55]. As a result, it potentially leading to either duplication of medicines; alternatively, patients not taking their prescribed treatments as directed; consequently, not gaining the most benefit from their medication [56]. These scenarios are exacerbated if pharmacists lack training on how to handle concerns with substitution and/or do not receive adequate



**Figure 2. Percentage prescribing frequency (% of total prescriptions) versus costs (% of total costs) for the five proton pump inhibitors in 2010.** Frequency in terms of overall items dispensed.



**Figure 3. Comparison of average costs per prescription (Rand) of originator (yellow) versus generic (blue) products for lansoprazole, omeprazole and pantoprazole.** Controloc® (Nycomed) and Pantoloc® (Nycomed) are identical originator molecules of pantoprazole but branded differently, therefore they are both again indicated as originator products.

Please see color figure at <http://www.futuremedicine.com/doi/pdf/10.2217/ce.14.70>

payment for providing relevant information to patients potentially limiting the time spent with them [31,55]. INN prescribing, apart from a limited number of well-known situations, is one way to address this as well as to obtain low prices for generics especially with increased transparency in the pricing of generics [15]. This has worked well in the UK with very high INN prescribing rates of 98–99% across a range of molecules [15].

We accept that the limitations of the study include the fact that there was no clinical information or diagnoses available in the database and that only patients served by the private healthcare sector in South Africa were included in the study. However, we believe that our findings are still valid and provide guidance to the authorities in South Africa in the future for the reasons we have documented.

### Conclusion

The authors have shown that multiple demand-side reforms in South Africa have appreciably increased the

prescribing of generics versus originators and single-sourced products in a class. However, additional measures are needed to further reduce the prescribing of single-sourced PPIs to levels seen in the UK. The reforms have also led to prices of generic PPIs at 36% to 68% of originator prices in 2010. Additional measures are needed to further lower generic prices to 10% or lower of originator prices to mirror the situation seen among some western European countries with their aggressive generic pricing policies. It is hoped that the findings and suggestions from this study will provide guidance to the authorities in South Africa regarding potential future measures they could consider to further improve prescribing efficiency.

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### Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

### Executive summary

- There have been multiple reforms in South Africa in recent years to encourage the prescribing of generics. This includes mandatory generic substitution and many medical aid schemes in South Africa only reimbursing the cost of the generic product.
- However, there are concerns with the long-term use of proton pump inhibitors (PPIs). In addition, there are concerns with the limited knowledge of their utilization patterns and expenditure in South Africa.
- Omeprazole was the most prescribed PPI, accounting for half of all PPIs prescribed (51%), followed by esomeprazole (20%) and lansoprazole (18%). Overall, patented (single-sourced) PPIs accounted for only 21.5% of total PPIs in 2010, which is comparable to western European countries with multiple demand-side measures to reduce the prescribing of patented PPIs.
- Low utilization of generic versus originator PPIs, with originator omeprazole accounting for only 1.8% of total omeprazole prescriptions and originator lansoprazole for only 1.4% of total lansoprazole prescriptions. This suggests policies to enhance the prescribing of generics in South Africa appear to be working.
- Patients received on average 1.21 different PPI active ingredients over the year and an average of 2.91 PPI prescriptions per year. This suggests that chronic prescribing of PPIs does not appear currently to be an issue in South Africa.
- There appears to be relatively high prices for generic PPIs in South Africa, that is, between 68 and 36% of the originator price, which could be due to 'branded generics.' This compares to low prices that have been achieved for generic PPIs in some European countries at between 2 and 10% of prepatent loss prices, which provides a goal for South Africa in the future.

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