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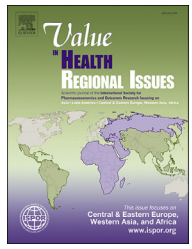

Brief Report

Pseudo-Generics in South Africa: A Price Comparison

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ABSTRACT

Background: The South African pharmaceutical market, like many other low- and middle-income countries, has long been synonymous with high medicine prices. In response to this, the government had instituted several policies to improve medicine pricing transparency and to lower medicine prices. Importantly among the new policies was the introduction of the single exit price mechanism and provisions for the increased uptake of generic medicines. Despite some early successes, the increasing presence of pseudo-generics in the South African pharmaceutical market appears to be hindering the process. **Objective:** This study sought to describe the price differentials among the originator, pseudo-generics, and true generics registered in South Africa in an effort to create consumer and prescriber awareness of this phenomenon. **Methods:** Private-sector medicine prices for the originator, pseudo-generics, and true generics were sourced from the South African Medicine Price Registry. **Results:** The study revealed that of most medicines with a true generic competitor (n = 10 of 14), the pseudo-generics were priced more than even the highest-priced generics. **Conclusion:** The increasing presence of pseudo-generics in the South African pharma market warrants further oversight and consumer and prescriber awareness.

Keywords: authorized generics, generic competition, pseudo-generics

Introduction

The current South African health system is still inherent to the highly fragmented and bureaucratic system that operated pre-democracy in 1994,[1] which has resulted in a 2-tier healthcare system (private and public) reflective of the country's divided history.[2]

The well-resourced private healthcare sector serves an estimated 15% of the population and is funded through medical aid contributions (66%) and out-of-pocket payments (29.7%).[3,4] The public healthcare sector, which is largely tax funded, services nearly 85% of the population.[5] These sectors are further differentiated by the pricing regulations that operate across each of them. Medicines in the public sector are procured via state tender schemes, whereas pricing of medicines in the private sector are governed by the Single Exit Price (SEP) mechanism.[2]

The SEP is a composite of the ex-manufacturer's price, logistics fee, and value-added tax. The SEP mandates that manufacturers sell their products at one price to all their customers (other than the State), regardless of the nature of the customer's order size and consumption levels.[6] Under the regulation, manufacturers are allowed to set their SEP, which may be raised once on an annual basis, as per a predetermined formula.[2] Manufacturers are not permitted to increase prices above the legislated SEP increase, unless granted permission from the Minister under exceptional circumstances.

Post-apartheid, in addition to improving medicine pricing transparency, the South African government sought to increase the use of generic medicines as a cost-saving mechanism.[7] This led to the mandatory offering of generic substitution by pharmacists, provided that a generic equivalent existed and the medicine was not on the Medicines Control Council non-substitutable list.[8]

Originator medicines are products that have been designed, developed, tested, and subsequently patented by a company to maximize economic gain, which may result from the availability of a new drug.[9] Patent protection and the sole monopoly of sales for a defined period allows the company to recoup costs incurred during research and development. Generic medicines can be defined as "medicines that contain the same active substances which are identical in strength or concentration, dosage form, and route of administration and meet the same or comparable standards that comply with the requirements for therapeutic equivalence as prescribed."[10] Generic medicines do not have to undergo the research and development expenditure incurred by originator

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firms and are thus offered on the market at much lower prices compared with originator medicines, with a 20% to 90% cost benefit.[11]

Generic medicines have become an important competitive force in the pharmaceutical market, gaining considerable market share from originator firms upon patent expiry.[12] In South Africa, the generic medicines policy, coupled with the increased registration of generic medicines and improved patient acceptance, has led to a steady increase in the use of generics.[2] Despite this, South African consumers continue to pay more for medication long past the patent expiry.[13] This, in part, is the result of the increasing occurrence of pseudo-generics in the South African pharma marketplace.[14]

A pseudo-generic is a medicine that has been launched by the originator company that is identical to the branded/originator medicine, often launched before patent expiry.[14] These products are sold at discounted prices to compete in the generic market without reducing the price of the originator medicine. Pseudo-generics, also referred to as authorized generics or branded generics, affect market dynamics because they represent a barrier to market entry of true generics. The price difference between a pseudo-generic and true generic medicines can be up to 40%. Despite this, pseudo-generics maintain market domination because patent or originator medicine manufacturers have a first-mover advantage that impedes natural competition as generics struggle to infiltrate the market. This ultimately results in increased medicine prices.[14]

Furthermore, first entry of pseudo-generics allows them to establish themselves as alternatives in the marketplace among prescribers and dispensers, often long before true generics appear on the market. These alternatives may thus be preferentially prescribed and stocked by doctors and pharmacists before generic medicines are launched in the country. The established relationship with originator companies also creates challenges for generic manufacturers, who now have to invest in marketing and brand building to promote their products and strengthen relationships with prescribers to increase product consumption.

Despite operating to a lesser extent in South Africa, independent generic manufacturers have begun to highlight their concerns regarding the negative economic impacts that pseudo-generics are creating in the generic medicine markets.[15] In South Africa under the current SEP regulation, originator manufacturers still have the freedom to set launch prices; however, the pricing committee is responsible for determining annual price increases in accordance with the SEP adjustment methodology. As a result, pricing of these medicines remains largely at the discretion of the manufacturer. In this regard, the government has proposed to introduce an external reference price system in which the prices of originator medicines will be compared with those in a basket of countries (Australia, Canada, New Zealand, and Spain, together with South Africa). These countries were chosen by the South African pricing committee based on 4 key criteria: having regulatory authorities that license and ensure the quality of medicines; having systems in place for the effective regulation of medicine prices, particularly through powerful purchasing structures; having accessible, structured pricing information that is regularly updated and reflective of the actual prices at which medicines are sold; and having implemented internationally accepted rules on patent and intellectual property rights protection. For generic medicines, the ex-manufacturer price is to be set at least 40% lower than the existing price of the originator medicine.[16] This legislative framework has been in the pipeline since 2006 but has faced stiff lobbying in implementation. If implemented, it would reduce originator medicine costs by around 25%.[17] It would thus be interesting to determine how many generics, including pseudo-generics, conform to the proposed policy.

The purpose of this study was to familiarize the reader with the presence of pseudo-generics in the South African market and to advocate for better regulation of these medicines.

Aim

This study aimed to compare price differentials among the originator, pseudo-generic, and highest- and lowest-priced generic for a basket of medicines and to determine what percentage of the basket of generics are priced at 40% lower than the originator medicine.

Method

This was a quantitative study based on private-sector prices of a basket of medicines. The basket (Table 1) consisted of all medicines registered in South Africa for which there was an originator, pseudo-generic, and generic alternative (where available).

Private-sector prices were sourced from the South African Medicines Price Registry, which is the official website that communicates drug prices as approved by the Pharmaceutical Economic Evaluation Unit of the Department of Health (as of September 19, 2018). Owing to the differences in pack sizes between originator and generic medicines, the SEP, inclusive of value-added tax per standard unit (ie, price per tablet or capsule) was computed. Descriptive statistics were generated. The proportional price differential between the originator and the corresponding pseudo-generic and the generic was calculated to determine how many generic medicines were 40% cheaper than the originator medicine.

Results

A total of 18 medicines were identified for this study. A division of the basket into their medication classes revealed the following categories: cardiovascular agents (n = 8), nervous system agents (n = 3), anti-infectives for systemic use (n = 2), alimentary tract and metabolism agents (n = 1), genitourinary system and sex hormone agents (n = 1), antineoplastic and immunomodulating agents (n = 1), musculoskeletal system agents (n = 1), and respiratory system agents (n = 1). Table 2 compares the SEP unit prices for the basket of medicines. For all medicines, with the exception of 4 (ie, bisoprolol 10-mg/hydrochlorothiazide 6.25-mg tabs, desloratadine 5-mg tabs, ramipril 2.5-mg tabs, and valsartan 80mg/ hydrochlorothiazide 12.5-mg tabs), the SEP of the pseudo-generic was consistently more than that of the highest-priced generic. An added observation was that for valsartan 160-mg and amlodipine 5-mg tablets, where there were no independent generic competitors, the pseudo-generic was priced equally to the originator.

Table 2 additionally describes the proportional price difference among the originator medicine, the pseudo-generic, highest-priced generic, and lowest-priced generic. Should external reference pricing have been implemented, all generic medicines would have been required to be 40% cheaper than the originator medicine. A small majority of the pseudo-generics (55.5%) and highest-priced generics (57.1%) and all of the lowest-priced generics would have conformed to this regulation.

Discussion

The presence of pseudo-generics in the South African pharmaceutical market seems to be prevalent across several medication categories. The highest proportion in this study emanated from

Table 1 – Drug class and ATC codes.

Active ingredients	Drug class	ATC code
Bisoprolol 5-mg tabs	Cardiovascular agents: beta-receptor blockers	C07AB07
Bisoprolol 10-g/hydrochlorothiazide 6.25-g tabs	Cardiovascular agents: beta-receptor blockers and thiazides	C07BB07
Desloratadine 5-mg tabs	Respiratory system: antihistamines for systemic use	R06AX27
Duloxetine 30-mg caps	Nervous system: serotonin–norepinephrine reuptake inhibitor	N06AX21
Etoricoxib 120-mg tabs	Musculoskeletal system: Cox-2 inhibitors	M01AH05
Imatinib 100-mg tabs	Antineoplastic and immunomodulating agents: protein kinase inhibitors	L01XE01
Itraconazole 100-mg caps	Anti-infectives for systemic use: triazole derivatives	J02AC02
Moxifloxacin 400-mg tabs	Anti-infectives for systemic use: fluoroquinolones	J01MA14
Quetiapine 100-mg tabs	Nervous system: diazepines, oxazepines, thiazepines, and oxepines	N05AH04
Ramipril 2.5-mg tabs	Cardiovascular system: ACE inhibitor	C09AA05
Tadalafil 20-mg tabs	Genitourinary system and sex hormones: drugs used in erectile dysfunction	G04BE08
Telmisartan 40-mg tabs	Cardiovascular system: angiotensin II receptor blockers (plain)	C09CA07
Telmisartan 40-mg/hydrochlorothiazide 12.5-mg tabs	Cardiovascular system: angiotensin II receptor blockers and diuretic	C09DA07
Tramadol HCl 37.5-mg/paracetamol 325-mg tabs	Nervous system: opioids in combination with non-opioid analgesics	N02AJ13
Valsartan 80-mg tabs	Cardiovascular system: angiotensin II receptor blockers (plain)	C09CA03
Valsartan 160-mg/Amlodipine 5mg tabs	Cardiovascular system: angiotensin II receptor blockers and calcium channel blockers	C09DB01
Valsartan 80-mg/Hydrochlorothiazide 12.5-mg tabs	Cardiovascular system: angiotensin II receptor blockers and diuretics	C09DA03
Vildagliptin 50-mg tabs	Alimentary tract and metabolism: dipeptidyl peptidase 4 inhibitors	A10BH02

ATC indicates Anatomical Therapeutic Chemical.

the cardiovascular class. This class currently has the largest number of generics and was ranked number 1 in the generic market share in South Africa.[18] Cardiovascular diseases are also South Africa's leading cause of non-communicable diseases, hence offering a lucrative avenue for pharmaceutical companies to invest in.[19] Research findings in Canada (where pseudo-generics make up approximately 25% of the market) reveal that the presence of pseudo-generics both deterred and slowed true generic entry and resulted in higher long-term medicine prices.[20] This is particularly unacceptable in South Africa, which is already synonymous with high medicine prices that have severely infringed on patients' human rights of accessing medical treatment.

Generic entry promotes competition and assists in reducing the overall price of a medicine.[21] Nevertheless, this phenomenon is only possible if there are a sufficient number of generic products on the market.[22,23] The presence of pseudo-generics in smaller medicine markets may be detrimental to price competition because it deters true generics from making the investment required to enter and slows the process of entry by competing generic firms, thus leading to higher long-run prices.[23] One of the reasons for this is that despite bypassing the large research and development costs incurred by originator firms, generic companies still incur large industry costs related to laboratory testing, comparative studies, and other supporting research before attaining approval from the South African Health Products Regulatory Authority. These additional costs affect the extent to which medication can be discounted by generic firms and the profits that are finally accrued. In light of this, one would expect that a pseudo-generic can be manufactured at a lower price for 3 possible reasons. First, the originator company possesses production experience with the line and hence can minimize the learning-by-doing costs associated with the pharmaceutical industry. Second, the pseudo-generic manufacturer already possesses the required documentation (via the originator company) and need not invest money in obtaining South African Health Products Regulatory Authority approval to enter the generic market. Finally, because the pseudo-generic is introduced by the patent holder, there are no legal obstacles to launching at the preferred time, even before patent expiration, and it can further enter the market at a time when it is most profitable to do so. Despite these savings, for most of the medicines sampled (14 of 18), the pseudo-generic was more expensive than even the highest-priced generic, indicating the strategy of these companies to maximize profits.

From our quick survey of these prices, the profit-maximizing strategy by manufacturers of pseudo-generics is already evident, particularly if we look at the example of combination valsartan 160-mg and amlodipine 5-mg tablets, where in the absence of any competition, the originator firm has priced the pseudo- generic and the originator at exactly the same price. This, however, was not noted for vildagliptin 50-mg tablets. This is consistent with studies conducted by King and Kavanos, who demonstrated that pricing variation may be sensitive to the class of generic medicines.[22] In the current study, it may be postulated that manufacturers of vildagliptin, despite not having any generic competition, are now competing with already long-established comparators in the treatment of type 2 diabetes mellitus.

Demand-side forces, owing to South Africa's pro-generic regulations, have led to a steady growth in the generic medicine market. Several medical insurers have adapted to promote generic substitution because members are often required to pay a co-payment if they are opting to take an originator medicine when a cheaper generic is available. This notably has created an impetus for the introduction of pseudo-generics onto the market owing to the profitability of the generic segment in South Africa. In addition,

Table 2 – A comparison of SEPs for the basket of medicines and price differentials among the originator, pseudo-generic, and highest- and lowest-priced generics.

Active ingredients	Originator SEP	Pseudo-generic SEP	Highest-priced generic SEP	Lowest-priced generic SEP	Number of registered brands	Price differential between originator and pseudo-generic (%)	Price differential between originator and highest-priced generic (%)	Price differential between originator and lowest-priced generic (%)
Bisoprolol 5-mg tabs	4.17	4.05	2.28	1.73	15	2.87	45.32	58.51
Bisoprolol 10-mg/ hydrochlorothiazide 6.25-mg tabs	5.93	3.46	3.79	3.21	5	41.65	36.09	45.87
Desloratadine 5-mg tabs	9.54	4.45	4.69	3.6	8	53.35	50.84	62.26
Duloxetine 30-mg caps	18.69	8.83	7.59	5.59	4	57.76	59.39	59.39
Etoricoxib 120-mg tabs	12.74	10.81	9.44	-	3	15.15	25.90	-
Imatinib 100-mg tabs	357.83	130.95	125.99	118.26	6	63.40	64.79	66.95
Itraconazole 100-mg caps	57.35	37.69	33.85	33.19	4	34.28	40.98	42.13
Moxifloxacin 400-mg tabs	56.05	41.48	37.51	31.26	8	25.99	33.08	44.23
Quetiapine 100-mg tabs	20.06	7.28	5.02	4.63	4	49.31	15.56	50.31
Ramipril 2.5-mg tabs	7.97	4.04	6.73	3.96	6	63.71	74.97	76.92
Tadalafil 20-mg tabs	122.94	97.21	-	-	2	20.93	-	-
Telmisartan 40-mg tabs	11.22	6.52	4.75	4.17	5	41.89	57.66	62.83
Telmisartan 40-mg/ hydrochlorothiazide 12.5-mg tabs	11.13	6.52	-	-	2	41.42	-	-
Tramadol HCl 37.5-mg/ paracetamol 325-mg tabs	3.21	2.73	2.2	1.88	4	14.95	31.46	41.43
Valsartan 80-mg tabs	10.1	5.04	4.25	3.08	6	50.01	57.92	69.50
Valsartan 160-mg/amlodipine 5-mg tabs	8.72	8.72	-	-	2	0	-	-
Valsartan 80-mg/ hydrochlorothiazide 12.5-mg tabs	10.1	6.22	6.22	3.55	5	38.42	38.42	64.85
Vildagliptin 50-mg tabs	5.85	2.88	-	-	2	50.77	-	-

Note. All prices are in ZAR. SEP prices are value-added tax inclusive. Medicine prices as of September 19, 2018.
SEP indicates Single Exit Price; ZAR, South African rand.

research reveals that an originator's profit drops by about 30% to 40% upon entry of a true generic version of a product.[14,24] This, together with demand-side changes, has induced originator companies to create pseudo-generics to ensure a continued price advantage. This is consistent with findings from a South African study, where it was shown that launching of a pseudo-generic was the dominant strategy by 11 of 14 manufacturers that were surveyed to both defend market share and capture a share of the generic market.[25] Nine of the 14 manufactures that had launched pseudo-generics admitted to wanting to launch before patent expiry to achieve first-to-market advantage. None of these 9 companies had contemplated lowering product price before expiration of the patent because they all wanted to avoid profit erosion while still under patent protection. For these manufacturers, lowering of prices was not seen as an effective way to deter entry because generics would always enter the market at a lower price.

The question thus remains, with the incentives in place to market pseudo-generics in South Africa, what are our options in regulating them? The proposed benchmarking presents 1 option, as all medicines would need to be priced at 40% cheaper than the originator. In addition to this, it may beneficial to ensure that originator firms are benchmarked as well. In this study, we observed that aside from the lowest-priced generics, a large percentage of pseudo-generics and highest-priced generic medicines did not conform to the proposed regulation, and hence its implementation would be impactful in reducing medicine prices.

The authors acknowledge that this study would have been strengthened by determining the market share of the 3 patent categories of medicines; however, financial resources were unavailable to obtain data on market shares and distribution units. In addition, further research is required to investigate if a generic paradox exists in the South African market, that is, despite the presence of cheaper generic alternatives, the prices of originator medicines continue increasing year after year. Finally, a qualitative evaluation of the perceptions of health professionals in relation to generics and pseudo-generics would be beneficial to ascertain practitioner awareness of the phenomenon and how it affects prescriber behavior.

In the interim, it is important to ensure that both patients and healthcare practitioners are made aware of the presence of pseudo-generics in the South African market. Greater efforts to educate these stakeholders should be undertaken to increase the transparency of their pricing.

Conclusion

Protecting the generic market is essential to the South African healthcare system. Although patients may often be naïve

regarding the differences in patency status and medicine pricing, it is essential for prescribers to create awareness of their differences to ensure improved affordability. Currently, pseudo-generics are poorly regulated in South Africa. The absence of said oversight may in the future result in a proliferation of these products populating the pharma landscape, particularly in the treatment of chronic diseases, thus increasing long-term medicine prices.

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