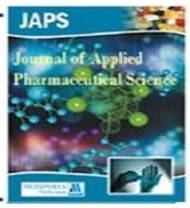
Journal of Applied Pharmaceutical Science
Available online at www.japsonline.com



ISSN: 2231-3354
Received on: 24-10-2011
Revised on: 08:11:2011
Accepted on: 24-11-2011

Generic competition and drug prices in the Malaysian off-patent pharmaceutical market

Omotayo Fatokun, Mohamed Izham Mohamed Ibrahim and Mohamed Azmi Hassali

Omotayo Fatokun,
Mohamed Azmi Hassali
Discipline of Social and Administrative Pharmacy, School of Pharmaceutical Sciences, Universiti Sains Malaysia, Penang 11800, Malaysia.

Mohamed Izham Mohamed Ibrahim
College of Pharmacy, Qatar University, Doha, Qatar.

For Correspondence
Omotayo Fatokun
Discipline of Social and Administrative Pharmacy, School of Pharmaceutical Sciences, Universiti Sains Malaysia, Penang 11800, Malaysia
Telephone: +60176442807

ABSTRACT

Promoting generic competition following patent expiration of innovator product is a key policy strategy in containing rising drug expenditure in both developed and developing countries. However, the effect of this measure on drug prices has not been specifically explored in Malaysia. This paper analyses the potential effect of generic competition on drug prices in the off-patent pharmaceutical market in Malaysia using retail price data of 28 off-patent multisource prescription medicines collected in a national medicines price survey in Malaysia. The relationship between number of registered brands of multisource medicines and their proportional prices was examined. The results show that the mean proportional price decreases as the number of brands increases, Pearson's r (6) =0.89, p=0.017 and the differences between the mean proportional prices among the various brands was significant, one-way ANOVA, F (5, 22) =3.68, p=0.014). However, further analysis using Tukey's post-hoc test analysis shows that the price differentials were not significant across all the brands of a given off-patent multisource product. The findings of this study revealed evidence of price lowering effect of generic competition among multisource drug products in Malaysia, though the effect was not observable across all drug brands.

Keywords: Generic medicines, generic competition, multisource products, off-patent, prices, Malaysia

INTRODUCTION

Generic competition has been advocated as a key means of containing the market price of drug products and is an important policy strategy for ensuring drug affordability and pharmaceutical cost containment, especially in developing countries (King and Kanavos, 2002; Nguyen et al., 2008). The concept of generic competition arises following the expiration of patent protection on innovator products and the eventual entry of equivalent generic versions. This entry makes more sources of supply available for the drug product and thus becomes a multisource drug product. Multisource drug products are "products marketed by more than one manufacturer that contain the same active pharmaceutical ingredient or drug substance in the same dosage form and are given by the same route of administration" (Shargel, 2009). The entry of generic medicines prompt price competition among the different brands of the off-patent product and helps lower the overall price of the drug product (Cook, 1998). However, the price lowering effect of generic medicines is only possible if there is sufficient number of generic products in the market (King and Kanavos, 2002; Nguyen et al., 2008). Several empirical studies (Caves et al., 1991; Cook, 1998; Frank and Salkever, 1992, 1997; Grabowski and Vernon, 1992; Kong , 2004; Lexchin, 1993; Saha et al., 2006), have shown that the greater the number of source of supply for a given off-patent

drug product, the wider is the price difference between the least expensive and the most expensive brand, and the lower the proportional price ratio or the generic-innovator brand ratio. Thus making it possible to obtain the least price for a given drug product (Dukes et al., 2003; King and Kanavos, 2002; Lexchin, 1993). Though majority of these studies have shown that the price of innovator products remain constant or increased following the entry of generic versions, there were however notable decrease in the generic-innovator price ratio or proportional price in the off-patent multisource market and the number of generic entrants was noted to be a key determinant of the observed trend (Caves et al., 1991; Kong, 2004; Saha et al., 2006).

In Malaysia, there have been a number of studies (Babar et al., 2005; Babar et al., 2007; Shafie and Hassali, 2008) that has examined drug prices either regionally or nationally. While these studies revealed substantial differences in prices between off-patent innovator and generic brands, the price-lowering effect of generic competition with respect to the number of available brands of the multisource pharmaceutical products in the overall market was not specifically explored. Therefore, the objective of this paper is to examine the potential effect of generic competition on the price differentials between the least expensive and most expensive brands of off-patent multisource drug products with respect to number of available brands of the multisource products. The overall aim is to provide evidence of the need of ensuring prompt market entry and availability of generic medicines after patent expiration on innovator products.

METHODS

Design

Secondary data analysis

Data sources

The price data was sourced from the 2006 national medicines price survey of health facilities in Malaysia as reported by the Malaysian medicines price bulletin, 2008 edition (Pharmaceutical Services Division, Malaysia, 2008). The bulletin provides private pharmacies retail price data on 28 multisource prescription medicines commonly prescribed for diseases with highest morbidity in Malaysia. As the actual price competition is predicted by the number of available sources for the drug preparations, the number of registered brands as at December 2006 for each drug preparation was obtained from the registered products database of the Malaysian national pharmaceutical control bureau (NPCB) and cross-referenced with the Malaysia Drug codes (Pharmaceutical Services Division, Malaysia, 2009).

Data analysis

Following the approach used in an earlier study (Lexchin, 1993), the effect of generic competition on drug prices was measured in terms of the difference between the maximum and minimum price for a multisource product according to the number of registered brands. For each multisource product, the proportional price, which was defined as the minimum price over the maximum price (minimum price/maximum price) was calculated. The drug products were then categorized according to the level of the overall competition (i.e. the number of brands for each drug product) and the mean proportional prices (in percentage) determined. The relationship between the mean proportional price (in percentage) and the number of brands was analyzed using correlation analysis and the difference between the mean proportional prices among the brand groups were analyzed using one-way ANOVA with Tukey's post hoc test following tests for normality and homogeneity of variances. It is hypothesized that as the number of brands increases, the lower the mean proportional price; and the level of competition increases the wider the price difference (proportional price) among the brands of a given multisource product. Data were analyzed using SPSS version 17. Significance level was set at $p<0.05$.

RESULTS

Table 1 list the 28 multisource drug products in our dataset, the therapeutic class to which they belong, their price differential, proportional price and the number of registered brands for each drug preparation. The largest therapeutic class in the sample is cardiovascular with 9 drug products, followed by anti-infective for systemic use and alimentary tract and metabolism with 5 drug products each. The total number of brands for the 28 drug products is 393, out of which cardiovascular has 110, alimentary and metabolism, 106 and anti-infective for systemic use, 65. Table 1 reveals considerable variability in the number of registered brands for each drug preparation. Expectedly, older generics medicines e.g. amoxicillin, atenolol, diclofenac, glibenclamide, gliclazide, mefenamic acid, metformin that have been off-patent several years back have more registered brands than newer off-patent medicines e.g. amlodipine, budesonide, cefuroxime, losartan, perindopril. A cursory look at Table 1 also shows that drug products with higher number of registered brands generally have lower proportional prices compared to drug preparations with lower number of registered brands. Thus suggesting that proportional price between the brands of a multisource product is inversely related to the number of available brands. To examine this relationship statistically, the drug products were categorized into 6 groups according to the number of registered brands for each product and their mean proportional prices calculated.

Table 1: Private pharmacies retail prices and number of registered brands of commonly prescribed medicines in Malaysia (2006)

Drug product(INN)	Therapeutic class[a]	Minimum unit price[b] *(RM)*	Maximum unit price *(RM)*	Difference between maximum and minimum unit price (%)	Proportional price[c] (%)	Number of registered brands[d]
Acyclovir tab 200mg	Anti-infective for systemic use	0.590	4.800	421	12.29	18
Amitriptyline tab 25mg	Nervous	0.250	0.300	5	83.33	3
Amlodipine tab 10mg	Cardiovascular	2.330	5.000	267	46.6	8

Amoxicillin caps/tab 250mg	Anti-infective for systemic use	0.150	1.500	135	10.00	22
Atenolol tab 100mg	Cardiovascular	0.230	2.900	267	7.93	27
Beclometasone inhaler 100mcg/dose	Respiratory	0.380	0.380	0.00	100.00	9
Budesonide inhaler 200mcg/dose	Respiratory	0.470	1.100	63	42.73	4
Captopril tab 25mg	Cardiovascular	0.700	1.720	102	40.70	10
Carbamazepine tab 200mg	Nervous	0.240	1.500	126	16.00	11
Cefuroxime tab 250mg	Anti-infective for systemic use	2.000	7.300	530	27.40	4
Ciprofloxacin tab 500mg	Anti-infective for systemic use	0.600	14.500	1390	4.14	18
Diclofenac tab 50mg	Musculoskeletal	0.200	2.000	180	10.00	25
Erythromycin susp 400 mg/5ml	Anti-infective for systemic use	0.080	0.130	5	61.54	3
Glibenclamide tab 5mg	Alimentary tract and metabolism	0.010	0.990	98	1.01	26
Gliclazide tab 80mg	Alimentary tract and metabolism	0.140	1.330	119	10.53	26
Loratadine tab 10mg	Respiratory	0. 40	1.500	110	26.67	27
Losartan tab 50mg	Cardiovascular	1.800	4.000	220	45.00	2
Lovastatin tab 20mg	Cardiovascular	0.700	1.500	80	46.67	16
Mefenamic acid tab/cap 250mg	Musculoskeletal	0.100	0.600	50	16.67	20
Metformin tab 500mg	Alimentary tract and metabolism	0.030	0.600	57	5.00	20
Metoprolol tab 100mg	Cardiovascular	0.300	1.800	150	16.67	13
Nifedipine tab 10mg	Cardiovascular	0.200	0.500	30	40.00	11
Omeprazole tab 20mg	Alimentary tract and metabolism	1.000	10.760	976	9.30	17[e]
Perindopril tab 4mg	Cardiovascular	1.000	2.830	183	35.34	6
Phenytoin cap 100mg	Nervous	0.030	1.350	132	2.22	3
Ranitidine tab 150mg	Alimentary tract and metabolism	0.100	2.800	270	3.57	17
Salbutamol inhaler 100mcg/dose	Respiratory	0.050	0.140	9	35.71	10
Simvastatin tab 20mg	Cardiovascular	0.700	4.000	330	17.5	17

Source: Malaysian medicine price bulletin, My.MedPrice Bulletin 2008[16] and the Malaysia drug products registration database available at http://portal.bpfk.gov.my/
RM= Malaysian Ringgit
[a]According to 1st level anatomical therapeutic classification (ATC) code
[b]Price per capsule, tablet, ml or dose.
[c] minimum unit price/maximum unit price
[d]Include both innovator and generic brands
[e]Include capsules as only the innovator brand exist as tablet as at end 2006

Figure 1and Table 2 illustrates the relationship between number of brands and the mean proportional prices of the multisource products. The results presented in Table 2 and Figure 1 shows that the mean proportional price declines with increasing number of brands. Correlation analysis shows that the relationship is linear and inverse, Pearson's r (6) =0.89, p=0.017. Overall, there was a strong, negative correlation between number of brands and mean proportional prices. This observation implies that as the number of brands for a given multisource product increases, the wider the price differentials between the most expensive and the least expensive brands as indicated by decrease in the mean proportional price.

Table 2: Descriptive statistics of the relationships between number of multisource brands and proportional prices

Number of brands (in categories)	Number of drug product (in each category)	Number of brands (grouped)	Proportional price (%)	
			Mean	Standard deviation
1-5	6	1	43.70	27.85
6-10	5	2	51.67	27.40
11-15	3	3	24.22	13.67
16-20	8	4	14.39	14.13
21-25	2	5	10.00	0.00
26-30	4	6	11.54	10.86

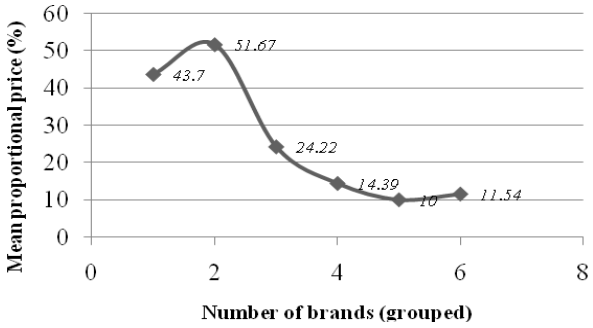


Fig 1: Relationship between mean proportional price and number of brands.

To examine the significance of the price differential between the most and least expensive brands of the multisource product, a one-way ANOVA was conducted to compare differences in the mean proportional prices among the 6 groupings of number of brands. As shown in Table 3, there was a significant difference between the mean proportional prices among the 6 brand groups. F (5, 22) =3.68, p=0.014. However, as shown in Table 3, further analysis with post hoc comparisons using the Tukey's HSD test indicated that the observed significant difference between the mean proportional prices among the 6 brand groups lies between mean proportional prices for groups of 2 (M=51.67, SD =27.40) and 4 brands (M =14.39, SD =14.13) as only these means were significantly different from one another (p=0.039). Other differences were not significant. Overall, these results suggest that as the number of brands for a given multisource product increases, the wider the price differentials among the brands. However, these differences do not occur across all the brands for a given multisource product.

Table 3: One way analysis of variance (ANOVA) of mean proportional prices with Tukey's pairwise comparisons between brand groups.

Number of brands (grouped)	Mean proportional price (%)	One-way ANOVA	Tukey's post hoc test					
		F (p-value)	Mean difference (*p*-value)					
			Number of brands(grouped)					
			1	2	3	4	5	6
1	43.70		-	7.967 (0.986)	(19.480) 0.748	(29.311) 0.119	(33.703) 0.353	(32.168) 0.178
2	51.67				(27.447) 0.452	(37.278) 0.039[b]	(41.670) 0.179	(40.135) 0.069
3	24.22	3.65 (0.014)[a]				(9.831) 0.978	(14.223) 0.970	(12.688) 0.960
4	14.39						(4.393) 1.00	(2.858) 1.00
5	10.00							(1.535) 1.00
6	11.54							-

[a]Between groups, (combined), N=6

[b] Tukey's post hoc test significant difference between mean proportional price of brand group 2 and 4

DISCUSSION

The results from our analysis support the hypothesized price-lowering effect of generic competition in the off-patent pharmaceutical market as shown by the decrease in the mean proportional price or the least expensive brand-most expensive brand price ratio as the number of brands of the multisource product increases. The result shows that the proportional price decreases from 0.52 to 0.10 when the numbers of brands increase from 1 to 2, and there was a significant difference in the overall price differentials. These findings are consistent with the results obtained in other studies (Caves et al.,1991; Cook, 1998; Grabowski and Vernon, 1992; Kong, 2004; Lexchin, 1993) that have examined the effect of generic market entry and competition on drug prices. For example, a study(Cook, 1998) commissioned by the US Congressional Budget Office observed that in a sample of 177 multisource drugs, the average generic-innovator price ratio (proportional price) decreased from 0.61 when there were only 1 to 5 generic manufacturers to 0.53 when there were 21 to 24 generic manufacturers of the same drug . Caves et al. (1991) similarly noticed that the average generic- brand price ratio of 30 pharmaceutical products that experienced generic entrants following patent expiration decreased from 0.60 to 0.20 when the average number of generics increased from one to 20. Lexchin (1993) also found that the price difference between generic brand and originator brand of multisource prescription drugs increased from 30% to 80% when the number of generic firms increased from 1 to 4. Though these earlier studies were conducted in a different pharmaceutical market environment, our findings and theirs could be a reflection of what is generally expected in unregulated markets where multiple sources for a given product freely engage in price lowering competition.

Though, our finding shows that the proportional price decreased as the number of brands for a given off-patent multisource product increases, the differences between the proportional prices were not significant across all the brands. The Tukey's post- analyses of variance of our sample data shows that the spread between the price of the least expensive brands and the most expensive brands only occurred significantly between the brand group 2 and 4, suggesting within the limit of our sample, that price lowering competition may not be present among all the available brands for a given multisource product. One theoretical explanation for this observation is that innovator brands (which are included in our sample) do not engage in price competition with generic brands (Kanavos et al., 2008), hence significant price dispersion may not be observed across all the brands. Generally, however, the more generic medicines are available in the marketplace, the lower is expected the overall drug price.

Policy implications

Our findings have implications for drug affordability and the overall pharmaceutical cost in Malaysia as it shows that treatments cost could be reduced by obtaining the least expensive brands of multisource drug products. This is especially important considering the "low- to middle-income status of the Malaysian economy, together with the high shares of out of pocket payment that makes demand for pharmaceuticals very income sensitive" (Business Monitor International, 2010). However, it instructive to state that majority of the drug sample used in our analysis are older off-patent drug products, which could accentuate the effect of generic competition (Kong, 2004), as they are more likely to have more brands available. Nonetheless, it is expected that the same price-lowering effect would be observed for newer off-patent drug products, as more generic brands enter the market (Grabowski and Vernon, 1996; Regan, 2008). However, the potential benefits to consumers and the healthcare system would depend on how prompt and sufficient the entry occur which in turn is a function of the existent and extent of barriers to entry (European Commission, Competition DG, 2009). Such barriers may result from regulatory interventions, incumbent's strategic behavior in the off-patent market and level of generic uptake resulting from the interaction between stakeholders such as providers, physicians, pharmacists, consumers and their incentive structures (Kanavos et al., 2008). In Malaysia, the cost associated with generic development and market entry particularly for locally produced generics presently constitutes a challenge, resulting in constrained generic competitiveness in the pharmaceutical market (Hassali et al., 2009) and consequently may cause rigidity in downward trend in price of medicines especially of newer off-patent medicines.

LIMITATIONS

Grouped data was used in the analysis to examine the overall effect of generic competition, as a comprehensive trend data on prices and number of generic sources of individual drug was not available, thus we were unable to examine the effect of generic competition on individual drug products. Additionally the findings of this study is may not be generalizable to the whole pharmaceutical market in Malaysia, as only the private retail price data was used.

CONCLUSION

Overall, this study shows that there is evidence of a potential price lowering effect of generic competition in Malaysia

which may have a positive impact on containing pharmaceutical cost. However, this situation could only be realized if prompt and sufficient market entry of generic medicines occur following patent expiration on innovator products.

CONFLICT OF INTERESTS

None Declared.

REFERENCES

Babar, Z. U., Ibrahim, M. I. M and Bukhari, N. I. Medicine utilization and pricing in Malaysia: The findings of a household survey. Journal of Generic Medicines, 2005; 3(1): 47-61.

Babar, Z. U., Ibrahim, M. I. M., Singh H., Bukahri., N. I and Creese A. Evaluating drug prices availability, affordability, and price components: Implications for access to drugs in Malaysia. PLoS Med., 2007; 4(3):e82.

Business Monitor International. Malaysia Pharmaceuticals & Healthcare Report Q3 2010, London; Business Monitor International: 2010.

Caves, R. E., Whinston, M. D and Hurwitz, M. A. Patent expiration, entry, and competition in the U.S. pharmaceutical industry. Brookings Papers on Economic Activity, 1991; 1-66.

Cook, A. How increased competition from generic drugs has affected prices and returns in the pharmaceutical industry, Washington; US Congressional Budget Office: 1998.

Dukes, M., Haaijer-Ruskamp F., de Joncheere C and Rietveld A. Drugs and money: Prices, affordability and cost containment, Amsterdam; IOS Press: 2003.

European Commission, Competition DG. Pharmaceutical sector inquiry final report, European Commission: 2009.

Frank, R and Salkever, D. Generic entry and the pricing of pharmaceuticals. Journal of Economics and Management Strategy, 1997; 6 (1): 75-90.

Frank, R and Salkever, D. Pricing, patent loss and the market for pharmaceuticals. Southern Economic Journal, 1992; 59(2): 165-179.

Grabowski, H and Vernon, J. Brand loyalty, entry and price competition in pharmaceuticals after the 1984 Drug Act. Journal of Law and Economics, 1992; 35: 331-350.

Grabowski, H and Vernon, J. Longer patents for increased generic competition in the US. The Waxman-Hatch Act after one decade. Pharmacoeconomics, 1996; 10:110-23.

Hassali, M. A., Yuen, K. H., Ibrahim, M. I. M., Wong, J. W., Ng, B. H and Ho, D. S. Malaysian pharmaceutical industry: Opportunities and challenges. Journal of Generic Medicines, 2009; 6(3): 246-252.

Kanavos, P., Costa-Font, J and Seeley E. Competition in off-patent drug markets: issues, regulation and evidence. Economic Policy, 2008; 55: 499-544.

King, D and Kanavos P. Encouraging the use of generic medicines: implications for transition economics. Croat Med J., 2002; 43(4): 462-469.

Kong, Y. The price premium of generic pharmaceuticals to brand-names and pharmaceutical price index. Applied Economics, 2004; 36 (7): 731-737.

Lexchin, J. Effect of generic drug competition on the price of prescription drugs in Ontario. CMAJ**,** 1993; 148 (1): 35-38.

Nguyen A., Kaplan, W. A and Laing R. Policy options for promoting the use of generic medicines in developing and transitional countries: a review paper, Geneva; World Health Organization: 2008.

Pharmaceutical Services Division, Malaysia. Malaysia Drug Code. 5th ed. Pharmaceutical Services Division, Ministry of Health Malaysia: 2009. Available at: http://www.pharmacy.gov.my/aeimages//File/BUKU_MDC_Edition_5-2009.pdf. Accessed 15 March, 2010.

Pharmaceutical Services Division, Malaysia. My.MedPrice Bulletin 2008. Pharmaceutical Services Division, Ministry of Health Malaysia: 2008. Available at: http://www.pharmacy.gov.my/aeimages//File/Bulletin_My._MedPrice_2008.pdf. Accessed 15 January, 2010.

Regan, T. L. Generic entry, price competition and market segmentation. International Journal of Industrial Organization, 2008; 26: 930-948.

Saha, A., Grabowski, H., Birnbaum, H., Greenberg, P and Bizan O. Generic competition in the US pharmaceutical industry. International Journal of the Economics of Business, 2006; 13 (1): 15-38.

Shafie, A. A and Hassali M. A. Price comparison between innovator and generic medicines sold by community pharmacies in the state of Penang, Malaysia. Journal of Generic Medicines, 2008; 6(1): 35-42

Shargel, L. Drug product performance and interchangeability of multisource drug substances and drug products. Pharmacopeial Forum, 2009; 35(3): 744-749.