

An Economic Evaluation of Generic Drug Entries in Turkish Pharmaceutical Market

Türkiye İlaç Pazarında Jenerik İlaç Girişlerinin Ekonomik Olarak Değerlendirmesi

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ABSTRACT

Background: The widespread use of generic medicines in Turkey will reduce pressure on the budgetary burden resulting from new treatments and facilitate access for more patients. Therefore, it is important to analyze the effects of the new generic drugs on the equivalent market in Turkey. The objective of the paper is to study the effects of generic entry on the price of the original drug and show the generic competition with increased number of generic drugs in Turkish Pharmaceutical Market.

Materials and Methods: We evaluated 46 equivalent groups and 256 medicines. We assessed the groups that generic equivalents of original products market entry after January 2007 for ten years period in Turkey. Unit prices (TL) were calculated with using monthly sales (TL) and monthly unit sales quantities obtained from Quintiles and Intercontinental Marketing Statistics database. In order to calculate the generic market entry effect in each generic equivalent group, we calculated the 12-month average unit price of original drug before first generic entry and we calculated the 12-month average unit price of original drug after the first generic entry.

Results: We observed that in this study, 39 original products average prices decrease was 25.85% [standard deviation (SD)±10.2%] and 10 products average price increase was 5.59% (SD±6.3) when a generic medicine first appeared in the market. On the evaluated equivalent groups, the original drug prices were significantly decreased when the generic drugs entered to the market.

Conclusion: This paper concerns the impact of generic competition on the market unit price ratio of original drugs and has shown that the effects of new generic entrance to market on original drug unit price are significant and enduring. But this effect ends with the entry of 6th generic drug. Therefore, if there are more than 6 generics there will be no more price drops.

Keywords: Generic drug competition, generic drug entry, Turkish pharmaceutical market

ÖZ

Amaç: Türkiye’de jenerik ilaçların yaygınlaşması, yeni tedavilerin bütçe üzerindeki baskısını azaltacak ve daha fazla hastanın erişimini kolaylaştıracaktır. Bu nedenle, yeni jenerik ilaçların Türkiye’deki eş değer pazar üzerindeki etkilerinin analiz edilmesi önemlidir. Bu çalışmanın amacı, jenerik girişinin orijinal ilacın fiyatı üzerindeki etkilerini incelemek ve Türkiye İlaç Pazarı’nda artan jenerik ilaç sayısı ile jenerik rekabetini göstermektir.

Gereç ve Yöntemler: Kırk altı eş değer grubu ve 256 ilaç değerlendirildi. Türkiye’de Ocak 2007’den sonra orijinal ürünlerin jenerik eş değerlerinin pazara giriş yaptığı gruplar on yıllık dönem için değerlendirildi. Birim fiyatlar (TL), IQVIA veri tabanından elde edilen aylık satış (TL) ve aylık birim satış miktarları kullanılarak hesaplanmıştır. Her bir jenerik eş değer grupta jenerik pazara giriş etkisini hesaplamak için ilk jenerik girişten önce orijinal ilacın 12 aylık ortalama birim fiyatını ve ilk jenerik girişten sonra orijinal ilacın 12 aylık ortalama birim fiyatı hesaplandı.

Bulgular: Bu çalışmada, bir jenerik ilacın piyasa içinde ilk ortaya çıktığında 39 orijinal üründe ortalama fiyat düşüşünün %25,85 [standart sapma (SS)±10,2 ve 10 üründe ortalama fiyat artışının %5,59 (SS±6,3) olduğunu gözlemledik. Değerlendirilen eş değer gruplarda, jenerik ilaçların piyasaya girmesiyle orijinal ilaç fiyatları önemli ölçüde düşmüştür.



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Sonuç: Bu makale, jenerik rekabetinin orijinal ilaçların piyasa birim fiyat oranı üzerindeki etkisiyle ilgilidir ve piyasaya yeni jenerik girişin orijinal ilaç birim fiyatı üzerindeki etkilerinin önemli ve kalıcı olduğunu göstermiştir. Ancak 6. jenerik ilacın girişi ile bu etki sona erer. Bu nedenle, 6'dan fazla jenerik varlığında daha fazla fiyat düşüşü olmayacaktır.

Anahtar Kelimeler: Jenerik ilaç rekabeti, jenerik ilaç girişi, Türkiye ilaç pazarı

Introduction

Turkey is one of the developing countries considering size of pharmaceutical industry. Turkish pharmaceutical market reached to double size on value basis from 2008 to 2017. This increase is proportional to the world pharmaceutical market. According to the Pharmaceutical Manufacturers Association of Turkey data, Turkish pharmaceutical market was TL 13.4 billion in 2010 and this number increased to TL 30.9 billion in 2018 (1). With the Health Transformation Program initiated in 2003 and the Social Security Reform carried out in 2006, there have been many developments affecting the pharmaceutical market and facilitating access to drugs.

In Turkey, pharmaceutical access to the market after obtaining registration granted by the Turkish Medicine and Medical Devices Agency (TMMDA).

In Turkey, drugs are allowed to enter the market after obtaining the license issued by the TMMDA.

Generic or original, all new drug prices are determined by TMMDA at the end of the marketing authorization process. An originator product can be priced up to 100% of the reference price until its first generic enters the market. Once a generic is introduced to the market both the originators and the generics are priced at 60% of the reference price.

Companies apply to social security institution (SSI) for reimbursement in order to enter the positive reimbursement list after marketing authorization is granted and retail price is set. Reimbursement decision is the responsibility of the inter-ministerial reimbursement commission (RC). For all pharmaceuticals, companies have to apply to the Medical and Economic Appraisal Committee (MEAC) with a reimbursement dossier which contains general information of the product, clinical data and literature review with pharmacoeconomic evaluation of the product. MEAC assesses all dossiers and declares its decision to RC which is responsible from the reimbursement decision and then RC finalizes the decision.

Due to the interventions developed for the increasing domestic production capacity in Turkey, analysis and evaluation of generic market were needed. The changes in the reimbursement policies made by the SSI (Alternative Reimbursement Applications, Localization Policies, etc.) have also been adopted by Ministry of Health and other

related stakeholders in over years. As in other European countries, the widespread use of generic medicines in Turkey and its encouraging will reduce pressure on the increased budgetary burden due to new treatments on public finance and facilitate easier access for more patients with the same budget. Therefore, it is important to analyze the effects of the new generic access on the equivalent market in Turkey.

The objective of the paper is to study the effects of generic entry on the price of the original drug and show the generic competition occur on the conditions of increased generic drug number situation.

Material and Methods

In the study, monthly data were used from Quintiles and Intercontinental Marketing Statistics (IQVIA) between the years 2007-2017, which was renamed IQVIA in 2017 and formerly known as QuintilesIMS (Quintiles and IMS).

An equivalent group is a group of drugs whose active substance(s), pharmaceutical forms and unit amounts of raw material are the same form. The list of equivalent groups, which are in the positive list was updated and published by SSI. In this study, 1.523 equivalent groups and 5.458 drug forms published by SSI and updated by IQVIA in August 2017 were evaluated. Some criteria were used to evaluate the generic entry into the market. The generic equivalent groups of the original products that entered the market in Turkey after January 2007 were evaluated. Due to database restriction, the previous period (monthly) of January 2007 could not be evaluated. Molecules in these groups will be referred to as original or generic depending on which product first entered the market. For this reason, equivalent groups with the original drug were selected as the first drug to enter the equivalent group. Those containing more than one original drug in the same group and equivalent groups containing only one drug in the equivalent group were also excluded from the study. Thus, 46 equivalent groups and 256 drugs were evaluated according to these criteria.

Unit prices were obtained by the ratio of IQVIA monthly sales (TL) to monthly box sales quantities. In order to calculate the generic entrance effect in an equivalent group, the 12-month average unit price of the original drug before the introduction of the first generic drug and the 12-month average unit price of the original drug after the introduction

of the first generic drug were calculated. The price change rate was calculated based on the price of the original product. This calculation continued for second, third, fourth and fifth generic entrance.

Ethics committee approval is not required for the study.

Statistical Analysis

The effect of the initial number of generic competitors was analyzed using analysis of variance (ANOVA) and post-hoc analysis was performed. Linear-by-Linear Association analysis was used to assess the relation between market life and price ratio of the original drug. Comparisons between original drug prices were made with using Student's t-test. Statistical analysis was made using IBM SPSS Version 22.0 and p-values of <0.05 were considered statistically significant.

Results

In Turkey, generic drug ratio is always more than the original drugs regarding unit sales. Beside this, generic drugs market share was only 30-35% of drug expenditure between 2011-2016 (Table 1).

We have 1.523 equivalent groups and 5.458 medicines. One thousand four hundred eighty-three of these are original medicine and 3.975 are generic. Nine-hundred sixty-one equivalent groups have original product as first drug in the group. Groups have 3.8 drug in average. Figure 1 shows distribution of the first generics of these groups by year of entrance. After an average of 8.89 years, there was an original drug entry into the generic competitive market.

The prices ratio of the 39 original products average prices decrease was 25.85% (SD±10.2%) and 10 products average price increase was 5.59% (SD±6.3) when a generic medicine

first appeared in the market. On the evaluated equivalent groups, the original drug prices were significantly decreased when the generic drugs entered to the market. Figure 2 shows the price ratio for original drugs when they first started generic competition as a function of the number of generic competitors. Having one or more generics was associated with additional decline in the price of the original drugs. This decline is statistically significantly decreasing as the number of generics increases ($p < 0.001$). As we noticed with post-hoc analysis of ANOVA having six or more generics was associated with a decline in the price of the original drugs compared to the situation where there was a single case ($p < 0.001$). The effect of the first generic entry was seen at 19.6%, but when the generic number increased to 6 or more, the fall in the original price was 3.8%.

Table 2 shows unit price ratios of original drug after generic entry according to market age of original drug. As for the correlation analysis, there is no statistical relationship between unit price ratios of the original drug after first generic entry according to market age of original drug ($p = 0.872$). Additionally, this situation is the same as other generic number.

Table 1. Annually market share of generic drug

	Generic drug ratio (unit)	Generic drug ratio (TL)
2011	52.9%	36.4%
2012	53.1%	36.0%
2013	53.6%	35.3%
2014	54.3%	29.4%
2015	55.1%	29.5%
2016	56.6%	30.7%

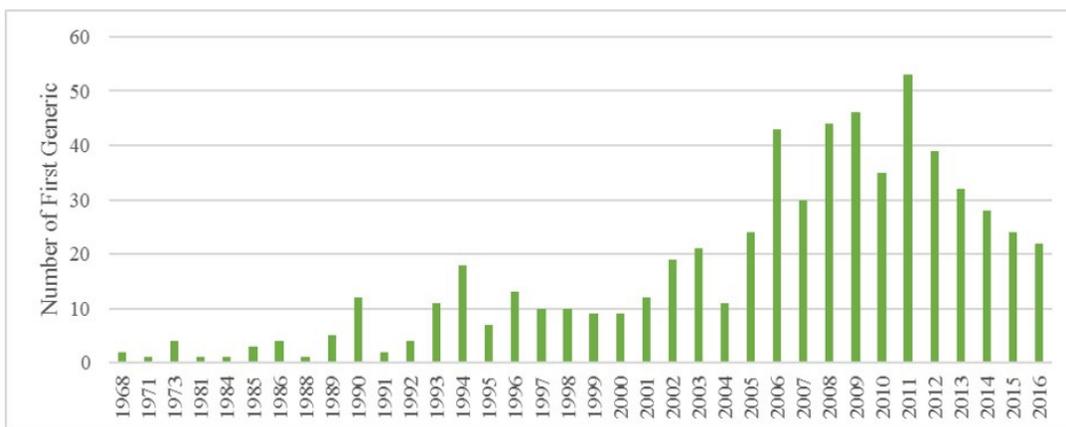


Figure 1. Annual first generic entrance, an equivalent group

Discussion

Physicians and pharmacists can persuade patients for the pharmacological equivalence of drugs and all drugs can switch between equivalent groups. There is a real switching cost between drugs. However, if a better product or a lower price is offered, price switching costs can be overcome. Although original products and generics have the same chemical substance, some consumers may have the impression that the brand-name product is better, so we do not assume homogeneity among the products, not because of their nature, but because of the perception of some consumers which is a consequence of brand loyalty (2,3).

Table 2. Unit price ratios of original drug after first generic entry according to market age of original drug

Market age of the drug (year)	Unit price ratios of original drug
2	-20.3%
3	-36.7%
4	-9.1%
5	7.7%
6	-11.6%
7	19.8%
8	-18.8%
9	-22.6%
10	-31.2%
11	-17.3%
	p=0.872

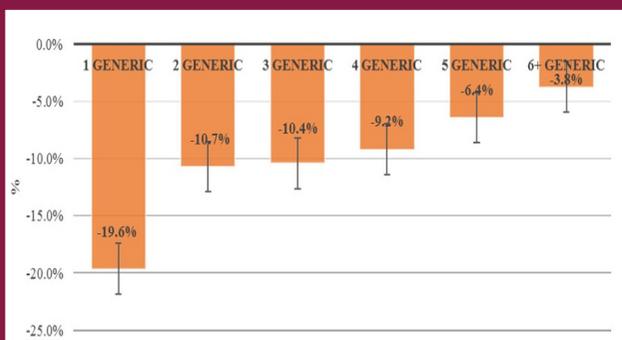


Figure 2. Effect of number of generic competitors on price of original product at time of introduction of generic competition. Unit price ratio of original products (one-year average unit price in when generic competition starts/one year average unit price in edition preceding introduction of generic competition; unit price is division of monthly unit sales to cost). Analysis of variance. *p<0,001 compared to six or more generics. Bars represent 95% confidence intervals

In Turkey, generic drug ratio is always more than the original drugs regarding unit sales. Beside this, generic drugs market share was only 30-35% of drug expenditure between 2011-2016. This paper concerns the impact of generic competition on the market unit price ratio of original drugs and our study has shown that the effects of generic drug entrance to market on original drug unit price are significant and enduring. According to study result, first decline of original drug price was due to the price policy in Turkey, the most important parameter affecting price change is the competition between products in the following years. But this effect ends up with more than 6 generic entries. While the data in this study is restricted to last 10 years, it is likely that being first generic into the market has more effects on original drug market share.

The lack of price competition may lead to increased costs in the market. When generics first became available having one generic was associated with a decrease in the price of the original drugs and compared to having two, three, four, five or six and more generic competitor, first generic has the highest effect.

There are lots of studies to explain the generic competition in literature. Frank and Salkever (2) looked at a sample of 32 drugs that lost patent protection. More competition among generic drug producers is found to cause price reductions for those drugs. Increased competition from generic drugs, however, is not accompanied by lower prices on branded drugs. Instead, their results suggest a small price increase on branded drugs.

In the study of Caves et al. (4) they investigate 30 drugs that lost patent protection between 1976 and 1987. The branded drug price declines with the number of generics. For the mean number of generic drugs, the original drug price declines by 4.5% only. At the same time generic prices are much lower than the brand name prices. This study has shown that average generic price is about 50% of the original drug price when three generic producers have entered the market.

Some of studies about generic competition have shown that the market share of the originator drug falls after patent expiry, but a small market share remains, despite the relatively higher price compared to generics (5,6,7).

In another study, it was shown that the generic effect of the brand loyalty is not prevented. The prices of generic drugs are lower than the prices of original drugs after the end of patent (3). Also Kanavos et al. (5) has shown that in the United States the average difference between original drug price and generic price up to 3 years after first entry is 80% and that the average generic drug entrance up to 3 years after first entry is 55%; in Germany, the original drug

price would have to decrease by 25-40% in order to regain a maximum of 45% of the market (7).

Brekke et al. (8) argue that the reference price application in original and generic competition is more effective than price ceilings.

Mats and Niklas (9) found that generic entry in Sweden led to a significant decrease in drug prices with the reference price system.

Grabowski et al. (10) found that generic medicines provide financial benefits to patients and reimbursement institutions in the United States. They came to the conclusion that generic competition caused significant price reductions in original drugs.

Aronsson and his colleagues showed that generic drug entry reduces market share of original drugs due to price competition and affects their prices (11).

Saha et al. (12) found that generic drug competition had a significant impact on important drugs with a high market share, especially called blockbuster, and the market share decreases resulted with lower prices of original drugs. It has been determined that this decrease in price is directly proportional to the increase in the number of generics.

Danzon et al. (13) have found that generics have reached a high market volume in the first year in the market, which is more likely the result of patients' interest and pharmacists' generic substitution.

Espin and Rovira (14) mentioned in the reports funded by the European Commission; it is easier to integrate use of generics with countries with single reimbursement agencies. According to the data obtained from the study, it has been proven in Sweden that generics saved around 760 million Euros between October 2002 and December 2005.

Mossialos et al. (15) reported that the introduction of ceiling prices for therapeutic groups in the United Kingdom with generic entry has resulted in savings of 474 million euros (2002) by reducing reimbursement prices. Puig-Junoy (16) done the literature review covering the years 2000 to 2009, it was determined that generic entry and competition in countries with ceiling price implementation were inadequate to lower prices, but prices of all drugs fell in groups with generic competition in countries with a reference price system. Wouters et al. (17) compared generic medicine markets and they found out that different generic incentives could affect use of generics such as pricing, prescribing, and substitution policies. Based on the studies price competition has direct effect on physicians' prescription and pharmacist dispense which resulted with increased generic use and cost-saving for payer.

Countries has policies to increase generic uptake. There are two important tools following; generic substitution and prescribing by International Non-proprietary Name (INN).

In a report published by World Health Organization, 45 countries were examined and in that 41 countries allowed generic substitution while it is obligatory in 14 of those countries. In the study it is examined that INN prescribing has been implemented in many countries and allowed in 24 countries and obligatory in 17 countries. Many countries clustered medicines into reference group based on therapeutic area and use internal reference pricing for reference groups. Patients has to pay difference in case if they wish to use expensive medicine in the reference group. The reference pricing system is financial incentive for patients to use generics in order to avoid co-payments.

Northern European Countries reduced prices with generic availability with tendering, results seem much more effective than more regulated generic policies not just for pricing also for generic uptake (18). But this policy may also result in high price differences between originator and generic in some therapeutic groups (19).

Twenty-five European countries support generic use by using INN prescribing and it is mandatory in 10 of them (20). Tenders and INN prescription system increase generic uptake and allow price competition between originator and generics. As mentioned in the article written by Kaplan et al. (21) government policies for pharmaceutical market that allow early entry to market for generics together with or without financial incentives for use of generics can achieve both increasing generic consumption and price competition.

Conclusion

This study concerns the impact of generic competition on the market unit price ratio of original drugs and has shown that the effects of new generic entrance to market on original drug unit price are significant and enduring. But this effect ends with the entry of 6th generic drug. Therefore, if there are more than 6 generics there will be no more price drops. While the data in this study is restricted to last 10 years, it is likely that being the first generic product to enter the market, has more effects on original drug market share.

Ethics

Ethics Committee Approval: Ethics committee approval is not required for the study.

Informed Consent: Not necessary.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: G.B., E.Ş.Y., Design: E.K.A., İ.M.V., H.G., Data Collection or Processing: E.Ş.Y., S.N., B.B., Analysis or Interpretation: H.G., İ.M.V., Literature Search: G.B., E.K.A., B.B., Writing: G.B., E.Ş.Y., A.B.

Conflict of Interest: No conflict of interest was declared by the authors.

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