



Prices of Generic and Originator Statins in Ukraine and Bulgaria

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Received: 14-06-2019; Revised: 26-07-2019; Accepted: 05-08-2019.

ABSTRACT

Cardiovascular diseases (CVD) prevalence is relatively high in Eastern and Central European countries. Within the EU, the share of all deaths result from CVD in men varies between 23% in France and 60% in Bulgaria. Outside the EU, the CVD mortality rate among men is the highest in Ukraine (59%). The study is retrospective, statistical analysis of the changes in generic and originator medicines' prices during 2013-2016. On total 7 international nonproprietary names (INNs) and 18 dosage forms (Anatomic therapeutic chemical (ATC) code C10AA) were observed. Generally, the difference in retail prices during 2013 - 2016 is higher for original medicines in both countries. A mean price and standard deviation are lower in Bulgaria. T-test shows that there is no statistically significant difference ($p > 0.05$) of price for all INNs, available on the market in 2013 and 2016 (except rosuvastatin price in Bulgaria ($p = 0.02$)). The prices in Ukraine are unsteady in the observed period. In Bulgaria they are more stable, despite the fact that there are no statistically significant differences in both countries. Rate of difference between the lowest and the highest priced dosage forms, established on the market is probably a results of health economic environment and manufacturer policy. Along with a lack of reimbursement policy it leads to limited patients' access to treatment. The small price difference between generic and originator medicinal products as well as affordable generics are very important in a country with high prevalence and mortality rate of CVD as it plays a crucial role for prevention, patients' adherence and treatment.

Keywords: Statins, generics, originator, the lowest price, the highest price.

INTRODUCTION

Cardiovascular disease (CVD) prevalence is relatively high in Eastern and Central European countries. Within the EU, the share of all deaths result from CVD in men varies between 23% in France and 60% in Bulgaria. In women it reaches to 70% in Bulgaria. The lowest age-standardized death rate for ischemic heart disease (IHD) is found in France, whereas the highest is in Lithuania.¹

Outside the EU, the CVD mortality rate among men is the highest in Ukraine about 59%. Among women it varies between 25% in Israel to 75% in Ukraine. The lowest mortality rate is found in Israel whilst the highest is in Ukraine (1,102 deaths per 100,000 in males; 429 deaths per 100,000 in females).

The global incidence of dyslipidemias is high. In the US, it is about 53%, whereas in Canada, the incidence is only 14%.^{2,3}

Percentage of CVD deaths attributable to high total cholesterol in males is 27.8 % in Bulgaria and 35.8 % in Ukraine.⁴ For females is found 26.5% in Bulgaria and 38.3% in Ukraine.⁵

Several clinical trials confirm that statins consumption reduces cholesterol level, coronary events and mortality. The decision to start statins therapy as a primary prevention should be based on a risk evaluation in

individual patients. According to the guidelines, the treatment of high-risk patients includes multiple strategies for enhancing of statins prescribing and utilization.^{6,7}

Statins prescribing generally increased from 2004 to 2015, with most patients receiving low- or moderate-intensity statins.⁸ In 2003 the highest level of consumption is found in Ireland and Norway, and the lowest one is in Italy. In all countries utilization continue to grow latest years- by 274% in Ireland and 56% in France from 2000 to 2003.⁹

Statins treatment as a primary prevention has a beneficial effect¹⁰ and it is also associated with a 26% reduction in all-cause mortality (hazard ratio (HR) 0.74, 95% confidence interval (CI) 0.63-0.88).¹¹

The goal of the study is to analyse the differences in prices of generic and originator statins in Bulgaria and Ukraine. It uses statistical approaches to determine the prices of available statins value and changes in Bulgaria and Ukraine.

MATERIALS AND METHODS

The study is retrospective, statistical analysis of the changes in prices between the lowest and the highest priced statins in BG and UA during 2013-2016. On total 7 international nonproprietary names (INNs) and 18 dosage forms of statins (Anatomic therapeutic chemical (ATC) code C10AA) are observed.



Retail prices of statins were collected from the official registry of the National council of pricing and reimbursement in Bulgaria¹² and market research system "Pharmstandard" of the company "Morion" in Ukraine.¹³

Results were analyzed using descriptive statistics and t-test. T-test was applied to test the statistical significance of the price variation for each individual INN during 2013-2016.

The difference between registered retail price in 2013 and 2016 is calculated in absolute term for each generic and branded medicinal product.

The prices were converted in €. The exchange rate is as follow: in Bulgaria 1 BGN = € 0.51. In Ukraine 1 € equals 10.92 UAH in 2013, 1 € equals 17.12 UAH in 2014, 1 € equals 24.36 UAH in 2015 and 1 € equals 28.28 UAH in 2016.

RESULTS AND DISCUSSION

The total number of compared dosage forms of statins differs in Bulgaria and Ukraine during the observed period:

Table 1: Number of observed products between 2013-2016

	2013/2014		2014/2015		2015/2016	
	Bulgaria	Ukraine	Bulgaria	Ukraine	Bulgaria	Ukraine
The total number of statins	28	29	28	31	28	30

The study compares the cheapest and the most expensive dosage forms of statins in Bulgaria and Ukraine. The price difference is illustrated in the following figures 1-4:

Figure 1: The highest and the lowest prices (Euro per package) in 2013 in Bulgaria

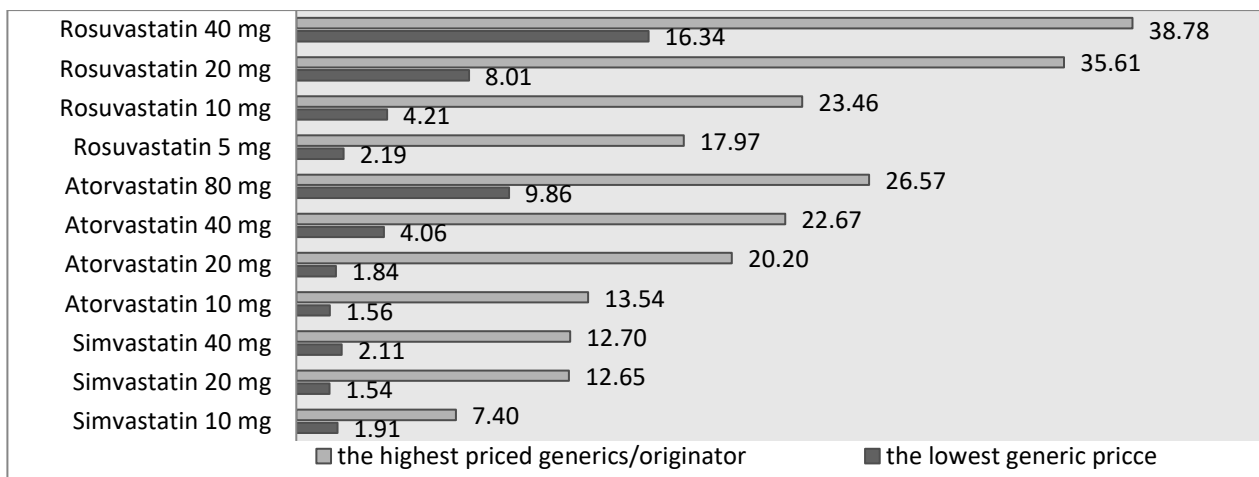


Figure 2: The highest and the lowest prices (Euro per package) in 2016 in Bulgaria

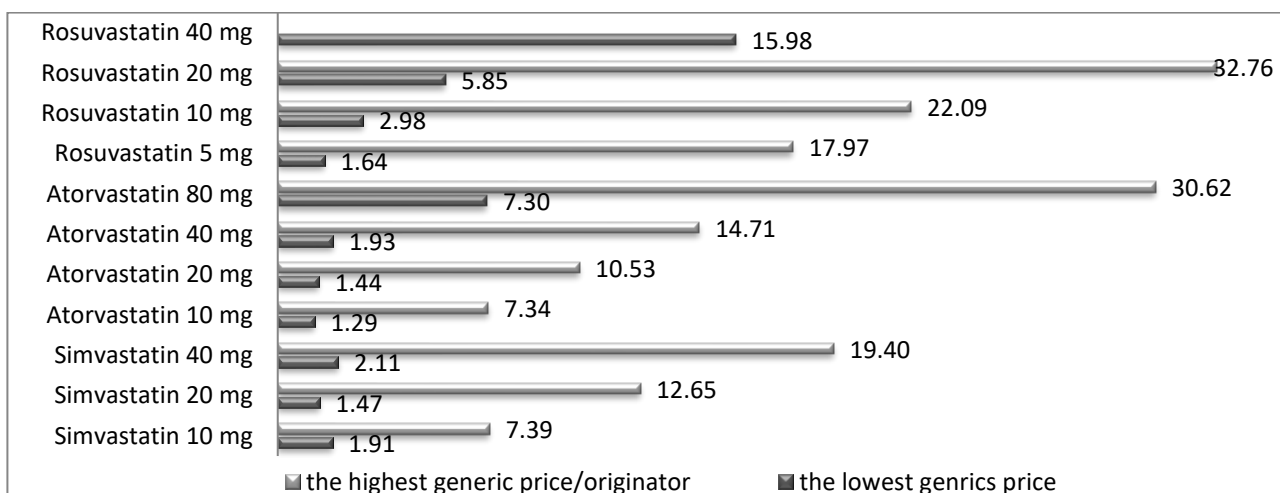
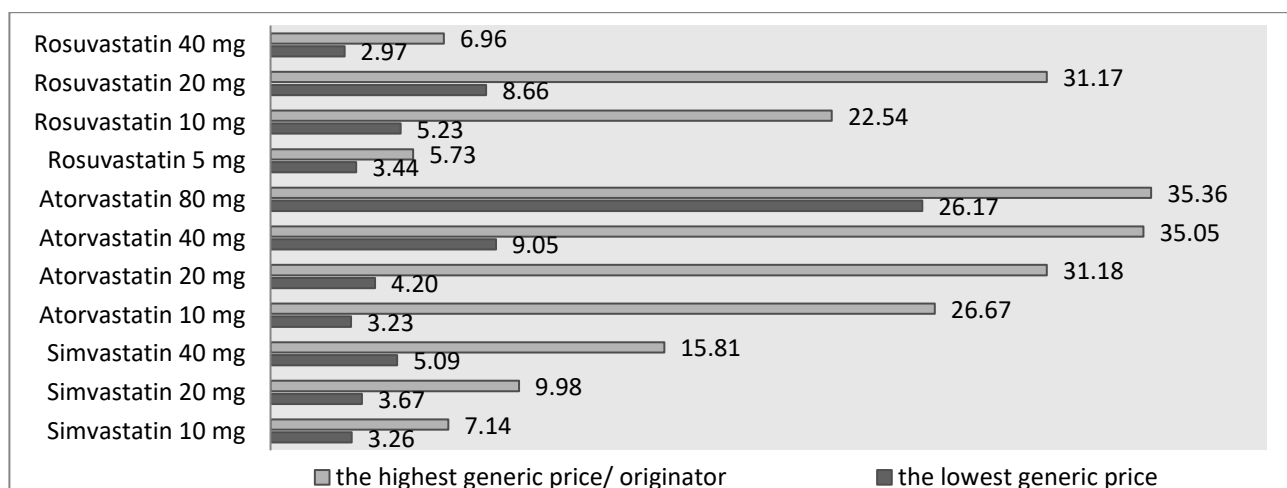
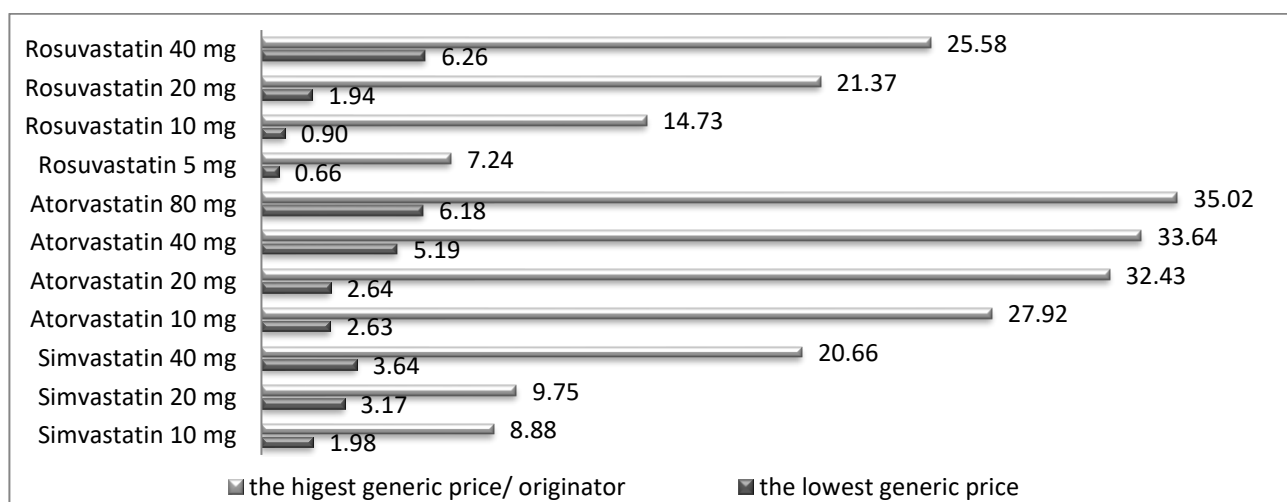


Figure 3: The highest and the lowest prices (Euro per package) in 2013 in Ukraine**Figure 4:** The highest and the lowest prices (Euro per package) in 2016 in Ukraine

Price value shows market changes in 2013 compared to that in 2016 (Table 2). Generally, the calculated difference in retail prices found as an absolute term is higher for original medicines in both countries during the observed period.

Table 2: Difference in the retail prices of statins during 2013-2016

Retail price difference between 2013 and 2016													
INN		BG	UA		BG	UA	INN		BG	UA		BG	UA
Simvastatin 10 mg	LP	0	1.28	HP	0	1.74*	Atorvastatin 80 mg	LP	2.556	19.99	HP	4.05*	0.34
Simvastatin 20 mg	LP	0.066	0.5	HP	0	0.23	Rosuvastatin 5 mg	LP	0.547	2.78	HP	0	1.51*
Simvastatin 40 mg	LP	0	1.45	HP	6.69*	4.85*	Rosuvastatin 10 mg	LP	1.231	4.33	HP	1.371	7.81
Atorvastatin 10 mg	LP	0.269	0.6	HP	6.196	1.25*	Rosuvastatin 20 mg	LP	2.155	6.72	HP	2.847	9.8
Atorvastatin 20 mg	LP	0.396	1.56	HP	9.673	1.25*	Rosuvastatin 40 mg	LP	0.361	3.29*	HP	-	18.62*
Atorvastatin 40 mg	LP	2.132	3.86	HP	7.961	1.41							

LP - The lowest generic price; HP - The highest generic price /originator; * - raising prices

The generic simvastatin 20 mg in Bulgaria and branded simvastatin 20 mg in Ukraine show the smallest variations.



The prices of statins were compared using descriptive statistics. As a whole, calculated mean prices and standard deviation are lower in Bulgaria than that in Ukraine. (Table 3)

Table 3: Mean price and standard deviation between 2013 and 2016

INN	Medicines strength (mg)	BG	UA
		Mean price (SD)	Mean price (SD)
Simvastatin LP	10	1.91(0.00)	2.62(0.91)
Simvastatin HP	10	7.40 (0.00)	8.01(1.23)
Simvastatin LP	20	1.50 (0.05)	3.42(0.35)
Simvastatin HP	20	12.65 (0.00)	9.87(0.16)
Simvastatin LP	40	2.11 (0.00)	4.37(1.03)
Simvastatin HP	40	16.04 (4.73)	18.24(3.43)
Atorvastatin LP	10	1.43 (0.19)	2.93(0.42)
Atorvastatin HP	10	10.44(4.38)	27.30(0.88)
Atorvastatin LP	20	1.64(0.28)	3.42(1.10)
Atorvastatin HP	20	15.36(6.84)	31.81(0.88)
Atorvastatin LP	40	2.99(1.51)	7.12(2.73)
Atorvastatin HP	40	18.69(5.63)	34.35(1.00)
Atorvastatin LP	80	8.58(1.81)	16.18(14.14)
Atorvastatin HP	80	28.60(2.86)	35.19(0.24)
Rosuvastatin LP	5	1.92(0.39)	2.05(1.97)
Rosuvastatin HP	5	17.97(0.00)	6.49(1.07)
Rosuvastatin LP	10	3.59(0.87)	3.07(3.06)
Rosuvastatin HP	10	22.77(0.97)	18.64(5.52)
Rosuvastatin LP	20	6.93(1.52)	5.30(4.75)
Rosuvastatin HP	20	34.19(2.01)	26.27(6.93)
Rosuvastatin LP	40	16.16(0.26)	4.62(2.33)
Rosuvastatin HP	40	19.39(27.42)	16.27(13.17)
Pravastatin1TM	10	5.44(0.00)	-
Pravastatin1TM	20	9.86(0.00)	-
Pitavastatin1TM	1	-	13.19(1.35)
Pitavastatin1TM	2	-	17.82(1.12)
Pitavastatin1TM	4	-	21.91(1.17)
Lovastatin1TM	20	3.66(0.21)	3.84(1.34)
Fluvastatin1TM	80	19.50(2.10)	NA

LP - The lowest priced generic; HP - The highest priced generic/originator; 1TM- one trademark is available on the market; NA- not applicable;

T-test was applied to verify the statistically significant difference between 2016 and 2013 prices of individual INNs. The result shows that a significant difference exist between rosuvastatin price in Bulgaria ($p = 0.02$). There were no statistically significant differences between prices of the other INNs ($p > 0.05$).

Larger price difference between generic and originator could affect medicines utilization. It also impacts primary

and secondary prevention and increases the probability of cardiovascular events and mortality.¹⁴ The cost savings of more than 50% could be generated if consumption is shifted from the originator to the lowest-priced generic equivalent, available on a market.¹⁵ Observational study covering 2006-2008 reveals that patients initiating generic statins therapy were more likely to treatment adherence.¹⁶



Our study found major differences between the most expensive and the cheapest dosage forms of statins (Figures 1-4). The price of 7 products remains unchanged and established mean price and SD show smaller variations in Bulgaria during the observed period. Rate of difference between the highest and the lowest priced dosage forms, established on a market is probably a result of health economic environment and manufacturers' policy.

Variations among the prices between originator and generic medicines are established in a study, comparing 16 countries (thus for gemcitabine lowest price difference between originator and generic is 1.4% in Belgium, but the highest difference found is 73.4% in Portugal; mycophenolate mofetil - 3.4% is lowest price difference in Norway and 71.7% in Netherlands) in 2012. The countries (Denmark, Sweden) with strong generic policies, based on competition and involving elements of enforcement, reveal higher differences between originator and generic prices.¹⁷

According to Bulgarian legislation the reimbursed medicines are divided into 3 Annexes of the Positive Drug List depending on the payment institution. Statins for ambulatory treatment are included in Annex 1, where reimbursement rate is 25% from the lowest priced medicine within the same INN. Statins used for hospital treatment are included in Annex 2, and the reimbursement level is 100%.¹⁸ The patients along with the cardiologists could take a decision for prescribed medicines. It improves patients' affordability and compliance, and leads to a wider statins utilization.

Register for reimbursed medicines have been created in July 2017 in Ukraine. Among the statins included in the Register of Medicinal Products is simvastatin only (5 trade names) with the established reimbursement 90% of the retail cost of the drug.¹⁹

Statistical analyses in our study confirm a previously found result that the prices in UA are unsteady- they grow up and decrease in the observed period. In Bulgaria they are more stable, although there are no found statistically significant differences in prices in both countries.²⁰

In spite a low rate of price decreasing in Ukraine, other factors as a difference between the cheapest and the most expensive dosage form, price variations and lack of clear reimbursement policy for the whole population, all together could affect total statins consumption and treatment results.

CONCLUSION

Rate of difference between the lowest and the highest priced dosage forms, established on a market is probably a results of health economic environment and manufacturer policy. Along with a lack of reimbursement policy it leads to limited patients' access to treatment.

The small price difference between generic and originator medicinal products as well as affordable generics are very

important in a country with high prevalence and mortality rate of CVD as it plays a crucial role for prevention, patients' adherence and treatment.

ABBREVIATIONS

BG -Bulgaria

UA - Ukraine

INNs: International nonproprietary names

SD: Standard deviation

CVD: Cardiovascular diseases

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Source of Support: Nil, Conflict of Interest: None.

