ANALYSIS OF THE CURRENT STATE AND THE DYNAMICS OF LIPID-LOWERING DRUGS IN THE PHARMACEUTICAL MARKET OF UKRAINE

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ABSTRACT

Objective: The purpose of this study was to analyze the assortment, availability, consumption status, and dynamics of lipid-lowering drugs in the pharmaceutical market in Ukraine.

Methods: Among the primary methods of research were applied the following: System and content analysis, marketing, logical and mathematical analysis, graphical mode, and also a way of detailed and abstract simulation and synthesis.

Results: The ratio of imported and domestic lipid-lowering drugs in Ukrainian pharmaceutical market was analyzed (imported lipid-lowering medicines account for 82% of the total number of this group in Ukrainian market, the share of local medications is 18%, respectively). The structural review and analysis of market characteristics of 5-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors group of medicines (sales, accessibility for people, and competitiveness) were conducted, and the most promising market segment for producers and distributors was identified. The most promising sector is rosuvastatin, which is characterized by an average sales volume with a tendency to increase and a high increasing profit.

Conclusion: Data on dynamics of the development of lipid-lowering drugs segment in the pharmaceutical market of Ukraine are systematized, which enables potential manufacturers to identify their market niche. As a result of the study, heavy dependency on imported lipid-lowering drugs in the pharmaceutical market of Ukraine was established, which determines low economic accessibility (especially in case of increasing in exchange rates) and physical availability (dependence on the regularity of shipments to Ukraine) for consumers. The most competitive medicines of atorvastatin and rosuvastatin group were determined, it was established that sales leader was pharmaceutical company KRKA dd, Novo Mesto (Slovenia) with generics Atoris and Roxer.

Keywords: Lipid-lowering drugs, Pharmaceutical market in Ukraine, Accessibility.

INTRODUCTION

It is common knowledge that cardiovascular diseases (CVDs) are the leading causes of death and disability in the world (more than 17 million deaths per year) [1,2].

The World Health Organization data indicate that CVDs, primarily stroke and coronary heart disease (CHD), are responsible for the death rate of about 48% of Europeans. At the same time, Ukraine has the most unfavorable dynamics of indicators and, to date, ranks first among European countries regarding mortality from circulatory system diseases and strokes [3,4].

Of particular, concern is the fact that more than 426,000 Ukrainians die annually from CVDs (an average of about 1000 people die daily). In the total mortality of Ukrainians over the past 3 years, CVDs account for 66% (in 2016, this figure was 67.3%), while in most European countries, this number does not exceed 50%. For example, the death rate in Ukraine due to a stroke in men is 18 times, and in women 14 times higher than in Switzerland [4].

According to numerous studies, almost 85% of CVDs develop as a result of circulatory disorders, which most often occur due to the accumulation of cholesterol in the duct of vessels (atherosclerosis). The lipid-lowering drugs prevent deposits of cholesterol plaques in the duct of vessels, thereby reducing the risk of many diseases, in particular, inhibitors of 5-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase (statins), whose high efficacy and safety have been demonstrated in some long-term multicentered studies [3,5-7].

In the global drugs market, it is the inhibitors of HMG-CoA reductase is the leaders in sales in recent years. It is explained by the fact that statin therapy is considered as a long-term strategy for primary and secondary prevention of CVDs and severe ischemic cases (sudden coronary death, myocardial infarction, and stroke) [7,8].

Ukraine is a part of the international community of countries that have set a goal to decrease mortality from CVDs by 25% in 2025. In this direction, in our opinion, the importance of educational work is unconditional, but the presence on Ukrainian pharmaceutical market a sufficient number of highly efficient and simultaneously available medicines, particularly lipid-lowering drugs, is an equally important component of timely medical and pharmaceutical assistance.

The purpose of our work was to analyze the medicines of the GMC-CoA reductase group of inhibitors in pharmaceutical market of Ukraine.

The rationale of the study dictates the need for accessibility of statins for patients who need lipid-lowering therapy, on the one hand, and providing information on market and demand trends for inhibitors of GMC-CoA reductase medications of local and foreign manufacturers, on the other hand.

It is known that the concept of social and ethical aspects of marketing is the most acceptable by the pharmaceutical industry, based on balancing three factors: Buyers (satisfaction of needs), enterprise (profit), and society (ensuring the continued welfare of the community as a whole). It is one of the fundamental principles of marketing management of a pharmaceutical enterprise to form the range of medicines following

needs of consumers [9]. Consequently, organized data on dynamics of the development of lipid-lowering drugs segment in pharmaceutical market of Ukraine enable potential manufacturers to identify their market niche.

The novelty of the study is a definition of competitiveness coefficient for trade names of medicines, characterizing the level of trust between doctors and consumers toward specific drugs and their manufacturers in dynamics.

METHODS

During the study, we used data from the information retrieval system Medicines State Register of Ukraine and the directory Compendium 2017 - Medicines [10,11].

Morion Company data (sales of medicines for 2013–2015) were used while analyzing the life cycle and computation of competitiveness.

Among the significant methods of research were the following: System and content analysis (study of local and foreign publications on the problem of circulatory system diseases, statistical data); marketing, logical, and mathematical analysis (analysis of drug market structure, definition of competitiveness); graphical method (visual, schematic representation of research results), as well as a process of descriptive and abstract simulation and generalization (formulation of conclusions).

RESULTS AND DISCUSSION

At the first stage of the study, it was found that the range of lipid-lowering drugs (C10A) in Ukrainian pharmaceutical market is represented by 82 trade names, taking into account dosage forms and without taking into account dosages (as of July 2017). The summarized data are presented in Table 1.

Among the groups of drugs with lipid-lowering effect, HMG-CoA reductase inhibitors are considered to be the most effective medicines, which are stable and significantly reducing the level of cholesterol and low-density lipoprotein, improving the clinical course of CHD, and

reducing the risk of fatal and non-fatal myocardial infarction and total mortality [5-8,12].

The subgroup of HMG-CoA reductase inhibitors (C10AA) on the pharmaceutical market of Ukraine is represented by five international generic drugs, among them: Simvastatin (C10AA01), lovastatin (C10AA02), atorvastatin (C10AA05), rosuvastatin (C10AA07), and pitavastatin (C10AA08) (Fig. 1).

The next stage of the study was a structural analysis, which revealed that the group of simvastatin (excluding doses) in Ukrainian market is represented by 10 trade names of medicines produced in 10 countries (Great Britain, Jordan, India, the Kingdom of Saudi Arabia, Portugal, Macedonia, Serbia, Slovenia, Ukraine, and Czech Republic). It is noteworthy that a drug of Ukrainian production – Vasostat - health is only 10% of the total market share.

Atorvastatin (excluding dosages) is represented by 27 trade names from 11 countries (Israel, India, Canada, Malta, Poland, Republic of Macedonia, Slovakia, Slovenia, USA, Turkey, and Ukraine). Ukrainian drug manufacturers produce four drugs, which are 14.8% of the total, 23 others are imported, which is 85.2%, respectively.

Rosuvastatin (excluding dosages) is represented by 24 trade names from 11 countries (UK, Hungary, Israel, India, Canada, Cyprus, Malta, Poland, Slovenia, Ukraine, and Czech Republic): 2 local drugs, which are 8.3% of the total, 22 others are imported, accounting for 91.7%, respectively.

Pitavastatin is represented by one imported medicine (France), lovastatin - 1 drug of Ukrainian origin.

Subgroups of fibrates (C10AB) and bile acid sequestrants (C10AC) are represented only by imported drugs (one each from Ireland and Canada, respectively); subgroup of other lipid-lowering agents (C10AX) - 2 imported (Hungary, Netherlands) and 3 local; a subset of other drugs (C10AX19) - 1 imported (Hungary) and 3 local drugs.

Table 1: Lipid-lowering drugs in the pharmaceutical market of Ukraine

| International non-proprietary name	Number of medicines by trade names	Countries manufacturers
C10A Lipid-lowering drugs, monocomponent		
C10A A HMG-CoA reductase Inhibitors		
C10A A02 Lovastatin	1	Ukraine
C10A A01 Simvastatin	10	Great Britain, Jordan, India, Kingdom of Saudi Arabia, Portugal, Republic of Macedonia, Serbia, Slovenia, Ukraine, Czech Republic
C10A A05 Atorvastatin	27	Israel, India, Canada, Malta, Poland, Republic of Macedonia, Slovakia, Slovenia, USA, Turkey, Ukraine
C10A A07 Rosuvastatin	24	Great Britain, Hungary, Israel, India, Canada, Cyprus, Malta, Poland, Slovenia, Ukraine, Czech Republic
C10A A08 Pitavastatin	1	France
C10A B Fibrates		
C10A B05 Fenofibrate	1	Ireland
C10A C Bile acid sequestrants		
C10A C01 Colestyramine	1	Canada
C10A X Other lipid-lowering drugs		
C10A X06 Omega-3-triglycerides including other esters and acids	5	Hungary, Netherlands, Ukraine
C10A X19** Other drugs	4	Hungary, Ukraine
C10B Lipid-lowering drugs, combination		
C10B A HMG-CoA reductase inhibitors in combination with other lipid-lowering agents		
C10B A02 Simvastatin and ezetimibe	1	Singapore
C10B A05 Atorvastatin and ezetimibe	2	India
C10B X HMG CoA reductase inhibitors, other combinations		
C10B X03 Atorvastatin and amlodipine	5	Hungary, Germany, Malta, Slovenia, Ukraine
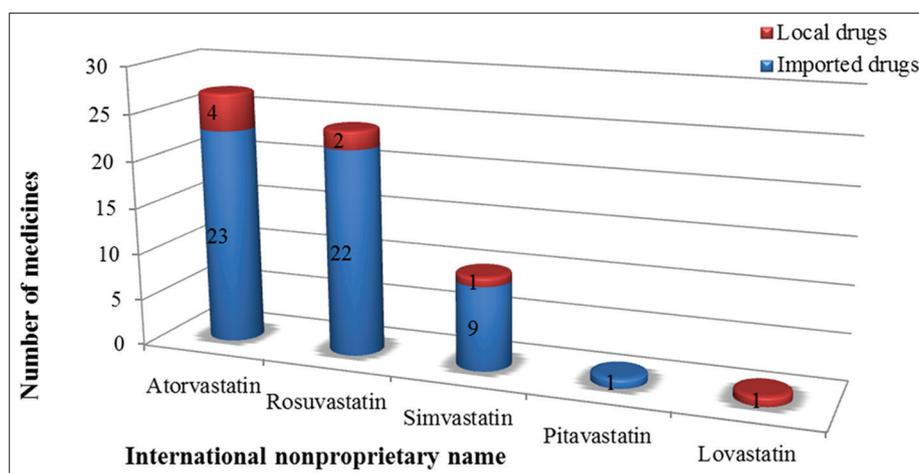
Fig. 1: Inhibitors of 5-hydroxy-3-methylglutaryl-coenzyme A reductase in the pharmaceutical market of Ukraine
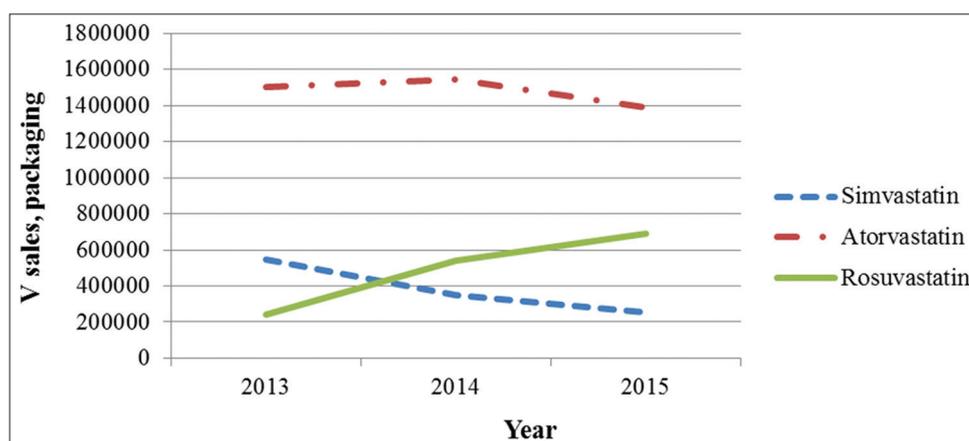

Fig. 2: Sales volumes and life cycle drugs group of 5-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors in the pharmaceutical market of Ukraine

Inhibitors of HMG-CoA reductase in combination with other lipid-lowering agents (C10BA) are represented by three imported drugs (India, Singapore), and with other combinations (C10BX) 4 imported (Hungary, Germany, Malta, and Slovenia) and one local drug. The summarized data are presented in Table 2.

The next stage of our study was an in-depth life cycle analysis of the drug groups HMG-CoA reductase international nonproprietary name, as a model of the market reaction in time. It has been revealed that simvastatin medicines are at the stage of the recession, atorvastatin is at the saturation stage, and rosuvastatin is in the growth phase (Fig. 2).

The data obtained indicate a redistribution of proportions of inhibitors of GMC-CoA reductase medications in prescriptions. Since 2013, there has been an increase in the number of orders for rosuvastatin medications (therefore, an increase in their sales) and a decrease in the number of prescriptions for simvastatin drugs (as a consequence, sales). It is worth pointing out that the data of our study is consistent with results obtained by COMCON Pharma-Ukraine as the part of a regular research project "PrIndex (Prescription Index). Monitoring prescribing of medicines" [13].

Despite the decline in sales of atorvastatin drugs, they continue to occupy a leading position in the market, as evidenced by Ukrainian researchers and global trends [14,15].

At the next stage of the study, to determine the state and sustainability of demand for the drug group under consideration, we calculated the
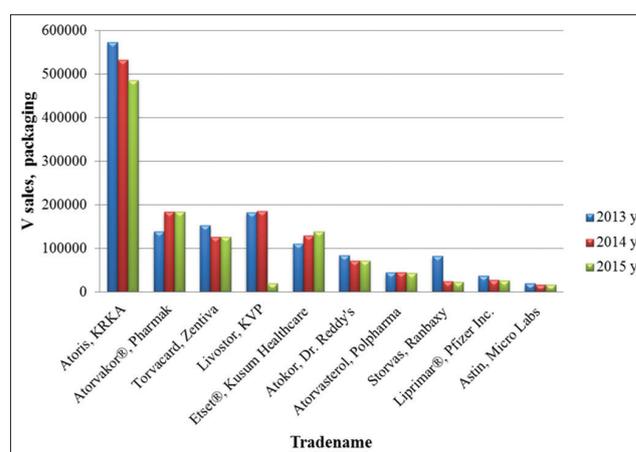

Fig. 3: Atorvastatin drugs are the leaders in sales in Ukrainian pharmaceutical market

competitiveness index, characterizing the level of attractiveness of OTC drugs for consumers, and the level of confidence in prescription medicines of doctors.

The calculation of competitiveness (C) was based on the drug sales volume (the number of packages was taken into account) in the period 2013–2015 according to the formula:
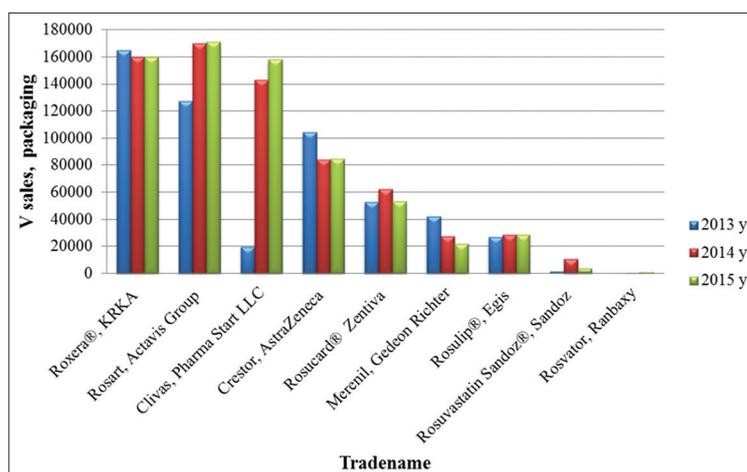
Fig. 4: Rosuvastatin drugs are the leaders in sales in Ukrainian pharmaceutical market

$$C = \frac{V}{\sum V \div q'}$$

Where: V - The volume of drug sales, the competitiveness of which is calculated;
∑V - Sales of drugs competitor;
q - The number of drugs competitors.

Based on the results of the calculations, medicine's groups of atorvastatin and rosuvastatin were identified as the most efficient, competitive, and safe (C >1). The summarized data are presented in Tables 3 and 4 and Figs. 3 and 4.

Based on the results of the analysis, it was revealed that only 6 out of the 27 trade names of the atorvastatin group registered in Ukraine are competitive. It was found that the most competitive drug from the atorvastatin group is Atoris (KRKA dd, Novo Mesto, Slovenia). Among other drugs, the coefficient of competitiveness of which is more than 1, the following are distinguished: Atorvakor® (Pharmak, Ukraine), Torvacard® (Zentiva, Czech Republic), Livostor, (Kiev Vitamin Plant, Ukraine), Etset® (Kusum Pharm, Ukraine), and Atokor (Dr. Reddy's Lab. Ltd, India). The summarized data are presented in Table 3 and Fig. 3.

Based on the results of the analysis, it was revealed that only 4 out of the 24 trade names of the rosuvastatin group registered in Ukraine are competitive. It has been established that the most competitive rosuvastatin drug is Roxera® (KRKA dd, Novo Mesto, Slovenia). Among other drugs, the coefficient of competitiveness of which is more than 1, the following are distinguished: Rosart (Actavis Group, Iceland), Clivas (Pharma Start, Ukraine), and Crestor (AstraZeneca UK Limited, United Kingdom). The summarized data are presented in Table 4 and Fig. 4.

Competitiveness defines, on the one hand, qualitative characteristics of medicines, and on the other hand - all significant purchase conditions and further use for the consumer. The results show that in the treatment with lipid-lowering medication consumers prefer to use drugs of medium and high price range predominantly of European production.

CONCLUSION

As a result of the study, it was found that imported lipid-lowering medicines account for 82% (67 trade names) of the total number of drugs of this group in Ukrainian market and are represented by manufacturers from 24 countries (the share of local medicines is 18%, respectively). The existing situation indicates a high dependency on imports in this segment of Ukrainian pharmaceutical market and determines low economic and physical accessibility for consumers.

Table 2: Countries - manufacturers of lipid-lowering drugs in the Ukrainian market

Manufacturer country	Number of medicines (%)
India	19 (23.17)
Ukraine	15 (18.29)
Slovenia	8 (9.76)
Hungary	4 (4.88)
Malta	4 (4.88)
Canada	4 (4.88)
Turkey	3 (3.66)
Poland	3 (3.66)
Czech Republic	3 (3.66)
USA	2 (2.44)
Israel	2 (2.44)
United Kingdom	2 (2.44)
Macedonia	2 (2.44)
Portugal	1 (1.22)
Saudi Arabia	1 (1.22)
Jordan	1 (1.22)
Serbia	1 (1.22)
Slovakia	1 (1.22)
Cyprus	1 (1.22)
France	1 (1.22)
Ireland	1 (1.22)
Singapore	1 (1.22)
Netherlands	1 (1.22)
Germany	1 (1.22)

It was discovered from the results of the analysis performed; the most competitive drugs of atorvastatin group are generics such as Atoris (Slovenia), Atorvakor (Ukraine), Torvacard (Czech Republic), Livostor (Ukraine), Etset (Ukraine), and Atokor (India). The most competitive medicines of rosuvastatin group are generics as Roxera (Slovenia), Rosart (Iceland), Clivas (Ukraine), and original medicine Crestor (Great Britain). The analysis found that in atorvastatin group of six competitive medicines two are of Ukrainian origin, which making a positive impact on the physical and economic availability of atorvastatin drugs. Moreover, in rosuvastatin group of nine drugs represented on the pharmaceutical market, only one is of Ukrainian origin that fact having a negative impact on the physical and economic accessibility of rosuvastatin group drugs to consumers. When analyzing market characteristics of drug groups, it has been established that the most promising segment is rosuvastatin, which is characterized by an average sales volume with a tendency to increase and a high increasing profit. The atorvastatin group is characterized by high sales but with a tendency to decrease and a top but declining profit. The simvastatin group is characterized by weak sales and low declining profits.

Table 3: Competitiveness of drugs with active substance atorvastatin in the pharmaceutical market of Ukraine (2013–2015)

Trade name	Coefficients of competitiveness			
	1.	2.	3.	To avg.
Atoris (Slovenia)	12.45	13.74	13.38	13.19
Atorvakor® (Ukraine)	2.08	3.37	3.53	2.99
Torvacard (Czech Republic)	2.32	2.2	2.29	2.27
Livostor (Ukraine)	2.83	3.4	0.48	2.24
Etset® (Ukraine)	1.64	2.25	2.54	2.14
Atokor (India)	1.21	1.2	1.23	1.21

Table 4: Competitiveness of medicines with active substance rosuvastatin in the pharmaceutical market of Ukraine (2013–2015)

Trade name	Coefficients of competitiveness			
	1.	2.	3.	To avg.
Roxera® (Slovenia)	3.08	2.42	2.45	2.65
Rosart (Iceland)	2.16	2.64	2.68	2.49
Clivas (Ukraine)	0.26	2.11	2.41	1.59
Crestor (United Kingdom)	1.67	1.03	1.13	1.28

DISCLOSURES

All authors have not disclosed potential conflicts of interest regarding the content of this paper.

REFERENCES

1. WHO. Cardiovascular Diseases (CVDs). Media Center, Fact Sheet. Geneva: World Health Organization. Available from: http://www.who.int/mediacentre/factsheets/fs317/en. [Last updated on 2017 2015 Jan 13; Last cited on 2017 Jul 21].
2. Andhuvan G, Ayyappan P, Sahana C, Poovizhi S, Sivasakthi K. Knowledge of modifiable risk factors of heart disease among patients with cardiovascular risk. Asian J Pharm Clin Res 2017;10:99-102.
3. Mendis S, Puska P, Norrving B, editors. Global Atlas on Cardiovascular Disease Prevention and Control. Geneva: World Health Organization; 2011.
4. Center for Health Statistics Ministry of Health of Ukraine. Center for Health Statistics Ministry of Health of Ukraine. Database of Medical-Statistical Information "Health for All" Kyiv: Center for Health Statistics Ministry of Health of Ukraine; 2009. Available from: http://www.medstat.gov.ua/ukr/news.html?id=203/. Ukraine. [Last updated on 2017 Aug 23; Last cited on 2017 Sep 20].
5. Affandi MM, Tripathy M, Majeed A. The prospect, promises and hindrances of statin base molecules: Look back to look forward. Int J Pharm Pharm Sci 2016;8:22-33.
6. Cahyawati PN, Sari DC, Romi MM, Arfian N. Simvastatin attenuates renal failure in mice with A 5/6 subtotal nephrectomy. Int J Pharm Pharm Sci 2017;9:12-7.
7. Jacobson TA, Maki KC, Orringer CE, Jones PH, Kris-Etherton P, Sikand G, *et al*. National lipid association recommendations for patient-centered management of dyslipidemia: Part 2. J Clin Lipidol 2015;9:S1-122.e1.
8. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, *et al*. Heart disease and stroke statistics--2015 update: A report from the American heart association. Circulation 2015;131:e29-322.
9. Mnushko ZM, Pestun IV, Timanyuk IV, Sofronova IV, Aliekperova NV. Management and Marketing in Pharmacy: The Textbook for International Students of Higher Pharmaceutical Schools in 2 Parts. Part II: Marketing in Pharmacy. Kharkiv: Dialog; 2016.
10. Derzhavnyy Reyestr Likars'kikh Zasobiv Ukrayiny. [Medicines State Register of Ukraine]. Kyiv: Ministry of Health of Ukraine; c2004-2017; Available from: http://www.drlz.kiev.ua/. Ukrainian. [Last updated on 2017 Jul 22; Last cited on 2017 Jul 22].
11. Morion 1999-2017: Spetsializovane Medychne Internet-Vydannya Dlya Likariv, Provizoriv, Farmatsevtiv, Studentiv Medychnykh ta Farmatsevtychnykh Vyshiv [Specialized Medical Online Edition for Doctors, Pharmacists, Students of Medical and Pharmaceutical Universities]. Kyiv; c1999-2017; ATC Classification. Available from: http://www.compendium.com.ua/. Ukrainian, Russian. [Last cited on 2017 Jul 22].
12. CR Consumer Reports. Consumer Reports; c2006-2017. Are You Taking the Right Treatment for Your High Cholesterol? 2014. Available from: https://www.consumerreports.org/cro/2014/03/treating-high-cholesterol-with-statins/index.htm. [Last cited on 2017 Jul 22].
13. Medpharmconnect. Kyiv: Medpharmconnect: The Medical Portal for Physicians; c2010. Company COMCON Pharma-Ukraine Conducted Monitoring of Statin Prescriptions; 2015. Available from: http://www.medpharmconnect.com/Isledovania/survey_results/20598.htm. [Last cited on 2017 Feb 16].
14. Hasan MM, Islam MF, Rahaman MM, Habib AM, Maniruzzaman M. An overview of the current status of prescribing pattern of statin molecules to prevent dyslipidemia in Bangladesh. Int J Innov Pharm Sci Res 2015;3:386-94.
15. Statista: The Statistics Portal. Top HMG-CoA Reductase Inhibitors by U.S. Prescription Market Share in 2013. Available from: https://www.statista.com/statistics/311999/cholesterol-lowering-drugs-by-us-prescription-market-share. [Last cited on 2017 Jul 22].