WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES
SJIF Impact Factor 6.647
Volume 6, Issue 6, 19-31 Research Article ISSN 2278 – 4357

INFLUENCE OF REGULATORY MEASURES AND MARKET POLICY FOR REIMBURSED MEDICINAL PRODUCTS ON THE VALUE, PAID WITH PUBLIC FUNDS IN BULGARIA IN 2015

Z. Mitkova*[1], M. Manova[1], M. Vasileva[2], B. Zidarova[2], D. Apostolova[2] and A. Savova[1]

[1]Faculty of Pharmacy, Medical University – Sofia, Bulgaria.

[2]National Council on Prices and Reimbursement of Medicinal Products, Bulgaria.

Article Received on
06 April 2017,

Revised on 26 April 2017,
Accepted on 16 May 2017,

DOI: 10.20959/wjpps20176-9374

***Corresponding Author**
Z. Mitkova
Faculty of Pharmacy,
Medical University –
Sofia, Bulgaria.

ABSTRACT

In Bulgaria large number of medicines yearly are included and excluded from Positive Drug List (PDL). It leads to different changes in the value per DDD paid with public funds (reference value) and utilization of medicines. The goal of the study is to analyze the main results from market policy of inclusion and exclusion of medicines in PDL as well as other factors leading to changes in reference value per DDD for all reimbursed medicines. The study is retrospective and observational analysis of Annex 1 and Annex 2 of Positive Drug List (PDL) in 2015. The changes in reference value per DDD, the rate of the decreasing or increasing of value were observed for all therapeutic groups in Annex 1 and Annex 2, where new medicines are included or excluded. We found that 109 new trademarks (belonging to 53 INNs), as well as 15 fixed dose combinations (belonging to 7 INN) in 2015 were included in Annex 1. 149 new trademarks, belonging to 67 INNs, were included in Annex 2, along with 16 fixed dose combinations (belonging to 7 INN). The number of excluded medicines is 60, belonging to 57 INNs from Annex 1, and 90 trademarks belonging to 85 INNs from Annex 2. On total the number of medicines in which the reference value is reduced is higher than medicines with the unchanged prices. The leading factor for decreasing the reference value in 2015 is a change of the price of the medicinal product within the group. It is mainly due to external reference comparison but also to generic and therapeutic competition. The next reason leading to decreasing the value is inclusion in PDL of generic medicines with lower prices.

KEYWORDS: pricing, reimbursement, reference value, generic competition.

INTRODUCTION

External reference pricing is the most used measure for controlling of prices of medicinal products and controlling the expenditures.[1, 2,3] Almost All EU member states apply external reference pricing for setting the prices of medicinal products although there are a lot of differences between country policies in terms of size of the reference basket, the level of prices comparison and the time of price revision. Also many countries apply additional policies for limiting the increasing expenditures for medicinal products (price cut or freeze, obligatory discounts etc.).[4,5] The published study show that external reference pricing (ERP) can lead to lower prices, but also there are a lot of differences in the prices between countries[6] The comparison between external reference pricing and value based pricing show that external reference pricing may lead to negative results on individual countries, especially those with low GDP.[7] Recently published study show that there is a need for changes in pricing policies and the external reference pricing is not enough for achieve long term sustainability.[8]

The main tool of reimbursement in pharmaceutical system is creation of positive list or formulary, which lists new drugs following predefined criteria. Various reimbursement criteria are used in European countries to cover national requirement depending on economic development.[9] Reference price system is often used to set common reimbursement values for equivalent products, so leaving patients to pay out-of-pocket the differences. In cases where generic substitutes or therapeutic alternatives are acceptable, purchasers in some markets obtain low prices using tendering processes, and this is more visible in countries with prevailing generic market.[10] Internal reference pricing, i.e. pricing drugs by reference to therapeutic comparators, is commonly used by payers and regulators to define the reimbursement value of generic drugs.[11] Internal reference pricing has impact mostly on public expenditures, but leads to increased out-of-pocket payments and is dependable of well-established system of additional insurance.[12] Inclusion of generic medicinal products in positive lists is a valuable tool for reducing the healthcare expenditures.[13,14] The decrease in expenditures is bigger in countries with high generic market share than in those with low generic market share.[15] Fast generic uptake however is subject to additional incentives for prescribers, pharmacists and patients.[16,17]

In Bulgaria, there is a positive drug list (PDL) which consists of four Annexes:

• (1) medicines paid by the National Health Insurance Fund (NHIF),

• (2) medicines paid by the budget of hospitals,
• (3) medicines paid by the budget of the Ministry of Health – medicines for the diseases which are out of the scope of Health Insurance, e.g. tuberculosis, HIV/AIDS, as well as vaccines for obligatory immunization,
• (4) prices of all medicines in PDL including: manufacturer price, wholesale and retail margins expressed as value and percentage, value of VAT.

Co-payment exists only for drugs listed in Annex 1, for outpatient care. The reimbursement levels are as following:

• 100% for the medicines for the diseases with a chronic course, leading to severe disruptions in the quality of life or disablement and requiring prolonged treatment,
• 75% for the medicines for diseases with a chronic course and widespread prevalence,
• 25% or 50% for the medicinal products for the diseases other than those mentioned above.

The reimbursement level depends of the type of the disease, the type of treatment (essential, symptomatic, palliative, etc.), clinical significance, and budget resources allocated for procurement of the medicine. The reimbursement level is based also on the product according to criteria for efficacy/therapeutic effectiveness, safety and pharmacoeconomic parameters.[18] The PDL is updated every month and pricing revisions for individual medicines are done every 6 months for original products and every 12 months for generics.

Medicinal products in PDL are listed according to INN and pharmaceutical form and the reference value is set based on the lowest price for defined daily dosage (DDD). The requirement for approving price of generic medicinal products is that the manufacturing price of generic medicine cannot exceed 70% of the manufacturing price of original medicinal product.

The changes in reference value per DDD are often like an indicator for the changes of medicines prices or the number of medicines within the therapeutic groups. We found that in Bulgaria high number of medicines were included and excluded for a year which influence prices of the reimbursed medicines and their utilization. If within the group only one generic medicine is reimbursed or reference product is excluded from PDL, reference value increase. We observe such changes and there is no regulatory approach to prevent exclusion of medicines. On the other hand when medicines with lower prices were included in the PDL this leads to decrease of reference value. The reason for the changes in reference value per DDD very often is result of dynamic market changes as well as therapeutic and generic

competition. An earlier research shows that a decrease of medicine prices and therefore the reference value, leads to significantly increase of their utilization.[19]

MATERIALS AND METHODS

The study is retrospective and observational analysis of the changes in reference value per DDD after an inclusion and exclusion of medicines from the Positive drug list (PDL) Annex 1 and Annex 2 in 2015 in Bulgaria. The annexes of the PDL were systematically reviewed and therapeutic groups were analyzed for the following changes – new trademarks included in PDL, new dosage forms, as well as INNs and trademarks excluded from PDL. The main reasons for changes in prices were analyzed within the year.

RESULTS AND DISCUSSION

Inclusion of medicines in PDL

The results show that in 2015 109 new trademarks, were included in Annex 1. The whole number of different dosage forms of fixed dose combinations (FDCs), belonging to 7 INN groups, is 15. 149 new trademarks, were included in Annex 2. As a whole 16 FDCs, belonging to 7 INN groups, were included (Table 1).

Table 1: Number of included medicines in 2015

Annex 1 Included in PDL:	**Number**
INNs monoproducts	44
Total number of FDCs*	15
Total number of included medicines	59
Annex 2 Included in PDL:	**Number**
INNs monoproducts	60
Total number of FDCs*	16
Total number of included medicines	76

*total number of included FDCs is based on number of all dosage variations.

Different changes are observed after inclusion of medicines in PDL. Most often new products lead to decrease of reference value per DDD of the group (Table 2).

We have observed the reasons leading to variations of the reference value - whether it is due to inclusion or exclusion of medicines within the therapeutic groups or is due to price revision (Table 2).

Table 2: Changes in reference value per DDD of medicines included in Annex 1 and Annex 2 in 2015

Annex 1					
Changes in reference value per DDD within the group after inclusion of medicines in PDL, % (59 INNs)		**Reason for the changes**			
		Exclusion of medicines from the group, %	**Inclusion of medicines in the group, %**	**Change in medicine prices within the group, %**	**Exclusion and inclusion of the same medicines from PDL, %**
Decreasing	61,02		27.78	72.22	
Increasing	11.86	42.86			57.14
No changes observed	27.12				

Annex 2					
Changes in reference value per DDD within the group after inclusion of medicines (76 INNs) , %		**Reason for the changes**			
		Exclusion of medicines from the group, %	**Inclusion of medicines in the group, %**	**Change in medicine prices within the group, %**	**Exclusion and inclusion of the same medicines from PDL, %**
Decreasing	64.47		42.86	57.14	
Increasing	9.21	42.86			57.14
No changes observed	26.32				

* New INNs included in 2015 are not shown in the table.

The main reason for decreasing of reference value per DDD is change of the price of medicines within the group (72.22% in Annex 1 and 57.14% in Annex 2) in 2015, result from price revision. Another reason is inclusion of new trademarks (27.78% in Annex 1 and 42.86% in Annex 2) in PDL at lower prices (e.g. a reference product).

The increase of reference value per DDD is observed only in 7 medicines (11.86%) and the main reasons is exclusion of the referent product from the group. Another reason is exclusion and inclusion of the same medicinal product from PDL in the same year.

We have observed that the trend is almost the same in both Annex 1 and Annex 2 - a reference value per DDD decreased at large number of products, 61,02% and 64.47% respectively, and it is due mainly to changes of prices of medicines within the therapeutic groups.

In terms of ATC classes of included products, the distribution is as follows:

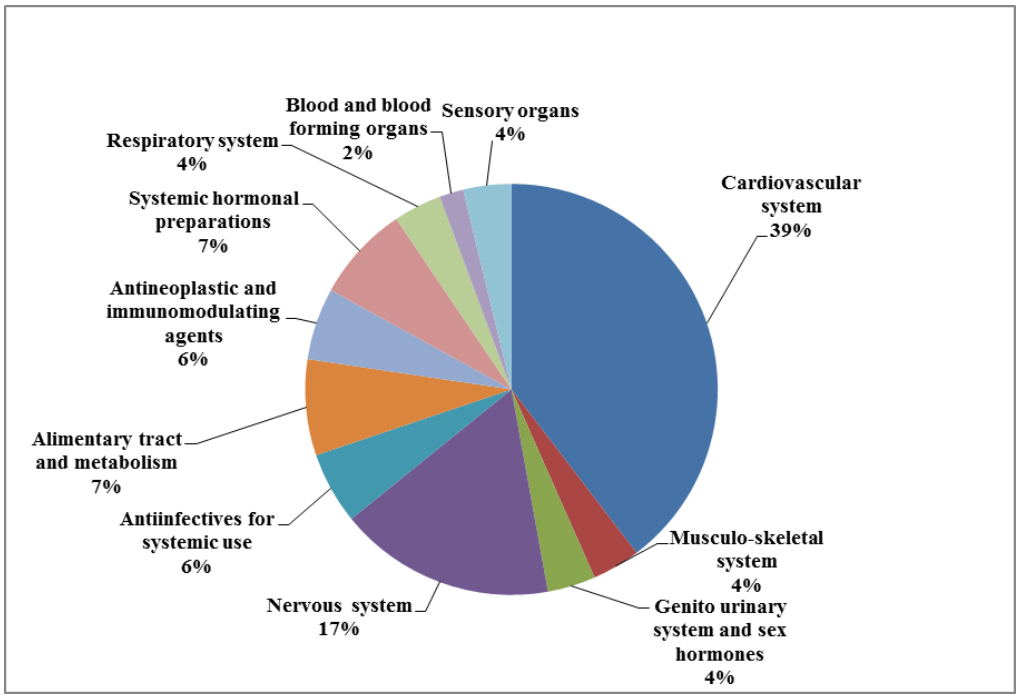

Figure 1: Medicines included in PDL -Annex1 according to ATC code

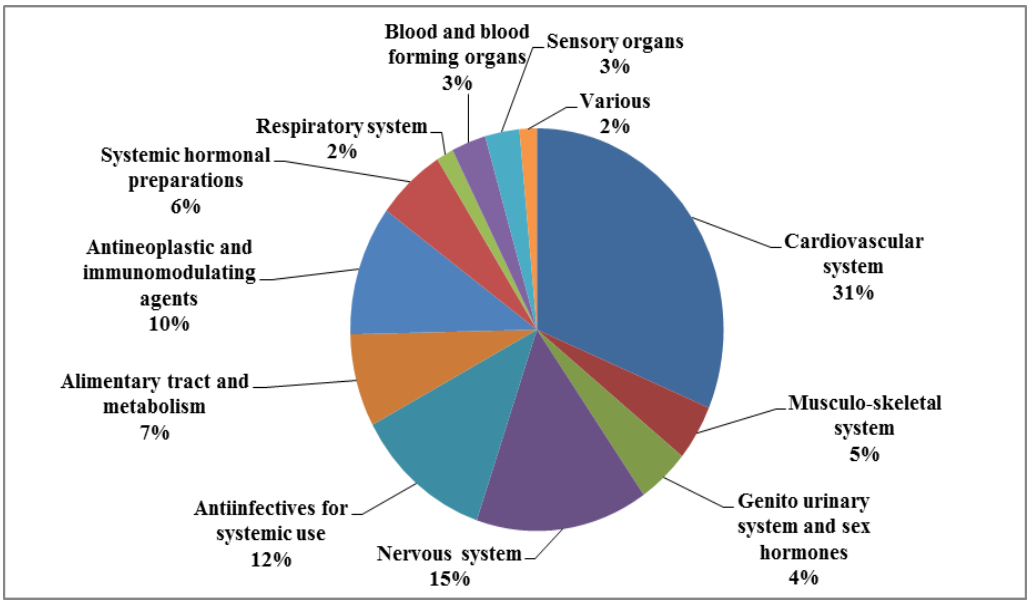

Figure 2: Medicines included in PDL- Annex 2 according to ATC code

The largest number of products are those acting on cardiovascular system (39% and 31% in Annex 1 and Annex 2 respectively), followed by the products acting on nervous system (17% and 15% in Annex 1 and Annex 2 respectively).

The first generic medicine is included in 7 groups in both Annex 1 and Annex 2 in 2015. The result is decrease of the reference value per DDD because of the regulatory requirement for

30% decrease of the price. This measure is used for control of the expenditures in Bulgaria and encourages generic utilization.

The study results shows that there are large number of included medicines in PDL which influence significantly reference value per DDD - the decrease is for over 60% of medicines.

Exclusion of medicines in PDL

The number of excluded medicines is 60, belonging to 57 INNs from Annex 1 and 90 belonging to 85 INNs from Annex 2. Within the groups of excluded medicines different changes were observed. We analyze the reasons for changes of the reference value per DDD - whether it is due to the exclusion of medicines or the changes are impacted from some market rules (Table 3).

Table 3. Changes in reference value per DDD of medicines excluded from Annex 1 and Annex 2 in 2015

Annex1					
Changes in reference value per DDD within the group after exclusion of medicines, %:		**Reason for the changes**			
		Exclusion of medicines from the group, %	**Inclusion of medicines in the group,%**	**Change in medicine prices within the group,%**	**Exclusion and inclusion of the same medicines from PDL, %**
Decreasing	31,66		15.79	84.21	
Increasing	23,34	71.42			28.57
No changes observed	45,00				
Annex 2					
Changes in reference value per DDD within the group after exclusion of medicines,%:		**Reason for the changes**			
		Exclusion of medicines from the group , %	**Inclusion of medicines in the group, %**	**Change in medicine prices within the group,%**	**Exclusion and inclusion of the same medicines from PDL, %**
Decreasing	28.89	7.69	11.54	80.77	
Increasing	25.56	73.91	4.35	4.35	17.39
No changes observed	45.55				

The number of products with increased reference value is smaller. We found that basic leading reasons for price reduction are changes in price of the products within the groups, the second leading reason is the inclusion of medicines at lower prices. The first generic medicine is included in both Annex 1 and Annex 2 in 7 INN groups. The final result is a decrease in reference value per DDD. Four of the products were excluded from the PDL and included again at higher price in the same year.

20 medicines used as reference for price calculation were excluded from Annex 1 and 27 medicines from Annex 2. It leads mainly to increase of the reference value. We found that in some group a reference product is excluded from the PDL, but new product with lower price is included as well as the price of the other products within the group are reduced at the same time. Finally the prices remain unchanged.

In terms of ATC class of the excluded products, the distribution is as follows:

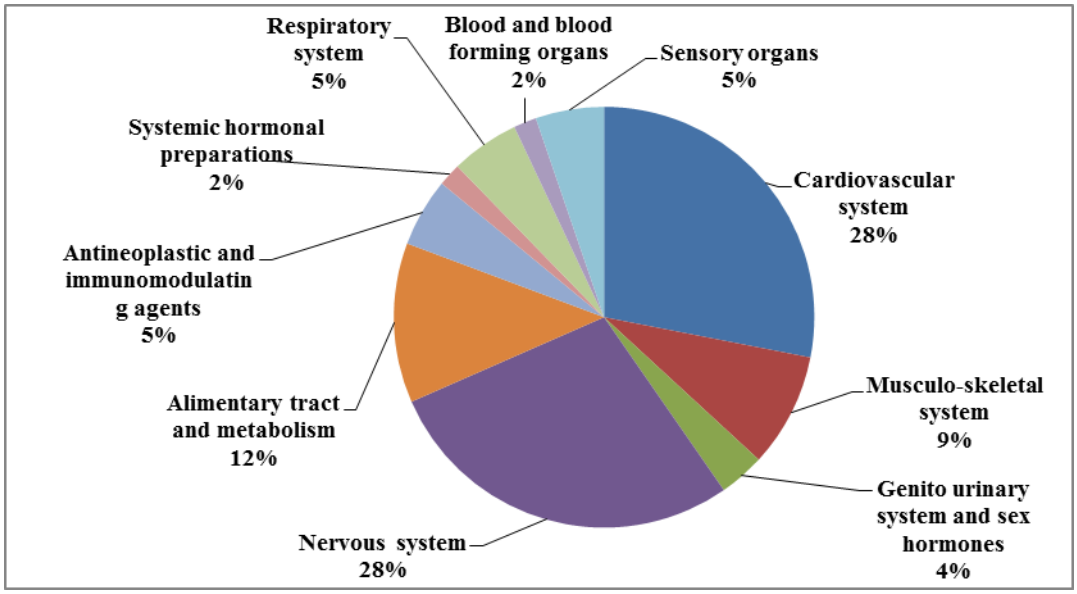

Figure 3: Medicines excluded from PDL- Annex 1 according to ATC code

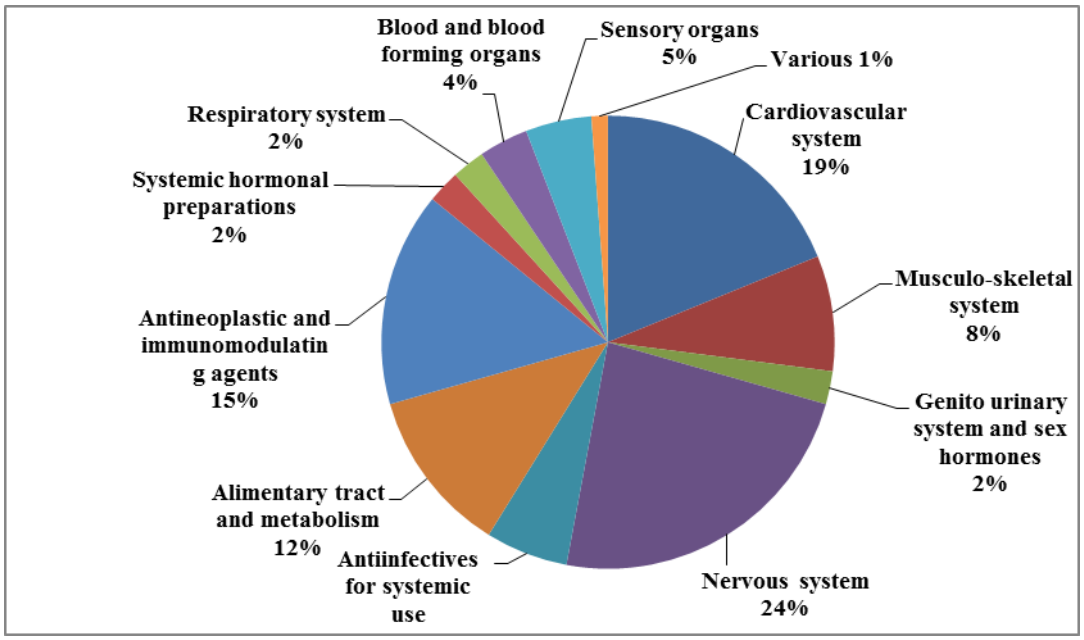

Figure 4: Medicines excluded from PDL –Annex 2 according to ATC code

The results shows that the highest number of excluded medicines acting on CVS (28% and 19% from Annex 1 and Annex 2 resp.), nervous system (28% and 24% from Annex 1 and Annex 2 resp.), as well as antineoplastic and immunomodulating agents (15% from Annex 2), alimentary system and metabolism (12% Annex 1 and Annex 2). The previous results for included in PDL products in 2015 show that in the group of the medicines acting on CVS, nervous system, antineoplastic and immunomodulating agents were included the highest number of products. These classes of medicines are dynamically developing in Bulgaria in 2015 with the largest changes in terms of the new trademarks and changes in the prices.

If we consider increase and decrease the prices, we can observe that the difference in the percentage for the following products are the highest (over 50%):

Table 3: The most significant changes in prices in 2015

INN	Increase of the reference value, %	Reason for the changes	INN	Decrease of the reference value, %	Reason for the changes
Excluded Annex 2			**Excluded Annex 2**		
Dorzolamide/ Timolol	67,3%	exclusion of medicines	**Risperidone**	-67,1%	change at the price
Methylprednisolone 40 mg	63,4%	exclusion of medicines	**Pantoprazole**	-61,4%	inclusion of medicines
Methylprednisolone 250 mg	76,7%	exclusion of medicines	**Anastrozole**	-68,7%	change at the price
Granisetron	69,3%	exclusion of medicines	**Excluded Annex 1**		
Ketoprofen	96,6%	exclusion of medicines	**Risperidone**	-67,1%	change at the price
Ibandronic acid	142,1%	exclusion of medicines	**Pantoprazole**	-61,3%	inclusion of medicines
Irinotecan	56,5%	exclusion of medicines	**Amlodipine**	-50,0%	change at the price
Venlafaxine	148,5%	exclusion of medicines	**Included Annex 1**		
Meropenem	91,4%	exclusion of medicines	**Donepezil**	-63,3%	change at the price
Sodium hydrogen carbonate	401,3%	exclusion of medicines	**Pantoprazole**	-61,3%	inclusion of medicines
Pantoprazole powder for solution	133,5%	exclusion of medicines	**Candesartan**	-66,3%	change at the price
Esomeprazole	78,5%	exclusion of medicines	**Thiamazole**	-70,8%	inclusion of medicines
Exenatide	50,0%	exclusion of medicines	**Pregabalin**	-56,5%	inclusion of medicines
Excluded Annex 1			**Included Annex 2**		

Dorzolamide/ Timolol	67,4%	exclusion of medicines	**Donepezil**	-63,4%	change at the price
Terazosin	100,6%	exclusion of medicines	**Pantoprazole**	-61,4%	inclusion of medicines
Venlafaxine	154,9%	exclusion of medicines	**Candesartan**	-66,4%	change at the price
Esomeprazole	78,6%	exclusion of medicines	**Thiamazole**	-71,0%	inclusion of medicines
Included Annex 1			**Pregabalin**	-56,5%	change at the price
Dorzolamide/Timolol	67,4%	exclusion of medicines	**Propofol**	-95,8%	Change at the price
Included Annex 2			-	-	-
Ketoprofen	96,6%	exclusion of medicines	-	-	-
Dorzolamide / Timolol	67,3%	exclusion of medicines	-	-	-

In 2015 the number of included products in PDL is higher than the excluded ones. On total number of the medicines of which the reference value per DDD is reduced is higher than the number of medicines with unchanged reference value. The number of products with increased reference value per DDD is the smallest.

As a whole the results from the study shows that in both groups included and excluded medicines, the leading factor for the decrease of reference value per DDD in 2015 is change of price of the medicine within the group. It is due to regulatory measures as price revision. The next reason leading to decreasing of reference value per DDD is inclusion in PDL of generic medicines with lower prices. We also have found that in the group of the included medicines reference value per DDD decreased in the largest number of INNs, but in the group of excluded medicines the price remain stable in large number of INNs. The increasing of the prices is a result mainly from the exclusion of medicines from PDL (e.g. a reference product).

CONCLUSION

In 2015 in Bulgaria different changes were observed in PDL regarding the inclusion and exclusion of medicines. If we observe all changes in the therapeutic groups we will find that both the regulatory measures and the control established on the prices are leading mainly to decrease of the reference value per DDD. The most dynamic changes were observed in medicines which affect CVS, NS and antineoplastic medicines. Despite the higher number of excluded medicines we've found that many new trademarks have been included too. The

results confirm that dynamic changes in PDL and prices of pharmaceuticals are contradictory, but in general this leads to increased availability and affordability to reimbursed medicinal products.

ACKNOWLEDGEMENTS

This study is financed with the support of Medical Science Council at the Medical University of Sofia – Contract 39 - Project № 398/19.01.2016.

REFERENCES

1. Kaplan, W. A., Ritz, L. S., Vitello, M., & Wirtz, V. J. (2012). Policies to promote use of generic medicines in low and middle income countries: a review of published literature, 2000–2010. Health Policy, 106(3): 211-224.
2. Leopold, C., Vogler, S., Mantel-Teeuwisse, A. K., de Joncheere, K., Leufkens, H. G., & Laing, R. (2012). Differences in external price referencing in Europe—a descriptive overview. Health policy, 104(1): 50-60.
3. Pieter Dylst, Arnold G Vulto, Steven Simoens. Reference pricing systems in Europe: characteristics and consequences. Generics and Biosimilars Initiative Journal (GaBI Journal). 2012; 1(3-4): 127-31.
4. Health Policy. 2016 Dec;120(12):1363-1377. doi: 10.1016/j.healthpol.2016.09.006. Epub 2016 Sep 20. Policy interventions related to medicines: Survey of measures taken in European countries during 2010-2015. Vogler S1, Zimmermann N2, de Joncheere K3.
5. Sabine Vogler, Lena Lepuschütz, Peter Schneider, Verena Stühlinger. Study on enhanced cross-country coordination in the area of pharmaceutical product pricing. December, 2015. Available at http://ec.europa.eu/health/sites/health/files/systems_performance_assessment/docs/pharmaproductpricing_frep_en.pdf.
6. South Med Rev. 2012 Dec; 5(2): 34-41. Epub 2012 Dec 27. Impact of external price referencing on medicine prices - a price comparison among 14 European countries. Leopold C1, Mantel-Teeuwisse AK, Seyfang L, Vogler S, de Joncheere K, Laing RO, Leufkens H.
7. Panos Kanavos, Elena Nicod, Jaime Espin, Stacey van den Aardweg. Short- and Long-Term Effects of Value-Based Pricing vs. External Price Referencing. January 2010. Available at: http://whocc.goeg.at/Literaturliste/Dokumente/FurtherReading/Short-%20and%20long-term%20effect%20of%20value-based%20pricing.pdf.

8. Vogler, S., Zimmermann, N., & Habimana, K. (2016). Stakeholder preferences about policy objectives and measures of pharmaceutical pricing and reimbursement. Health Policy and Technology, 5(3): 213-225.
9. World Health Organization 2015. Access to new medicines in Europe: technical review of policy initiatives and opportunities for collaboration and research. March 2015.
10. Dylst, P., Vulto, A. and S. Simoens (2011a), 'Tendering for outpatient prescription pharmaceuticals: what can be learned from current practices in Europe?', Health Policy, 101(2): 146-152.
11. OECD Health Policy Studies Pharmaceutical Pricing Policies in a Global Market OECD 2008 Available from: www.oecd.org/publishing/corrigenda.
12. Carone, Giuseppe and Schwierz, Christoph and Xavier, Ana (2012): *Cost-containment policies in public pharmaceutical spending in the EU.* Published in: European Economy-Economic Papers, Vol. ISSN 1, No. 461 (14. September 2012): pp. 1-64.
13. Vogler, S. (2012), 'The impact of pharmaceutical pricing and reimbursement policies on generics uptake: implementation of policy options on generics in 29 European countries-an overview.', Generics and Biosimilars Initiative Journal (GaBI Journal), 1(2): 93-100.
14. Brian Godman, William Shrank, Bjorn Wettermark, Morten Andersen, Iain Bishop, Thomas Burkhardt, Kristina Garuolienè, Marija Kalaba, Ott Laius, Roberta Joppi, Catherine Sermet, Ulrich Schwabe, Inês Teixeira, F. Cankat Tulunay, Kamila Wendykowska, Corinne Zara and Lars L. Gustafsso (2010). Use of generics—a critical cost containment measure for all healthcare professionals in Europe?. Pharmaceuticals, 3(8): 2470-2494.
15. Dylst P, Simoens S. Does the market share of generic medicines influence the price level?. Pharmacoeconomics. 2011 Oct 1; 29(10): 875-82.
16. Simoens, S. (2013). Sustainable provision of generic medicines in Europe. Report for the European Generic Medicines Association.
17. Dylst P, Vulto A, Simoens S. Demand-side policies to encourage the use of generic medicines: an overview. Expert review of pharmacoeconomics & outcomes research. 2013 Feb 1; 13(1): 59-72.
18. Ministry of Health. Ordinance on the terms, rules and procedure for regulation and registration of prices for medicinal products, *Effective 30 April 2013* Adopted by Council of Ministers Decree No. 97 of 19 April 2013 *Promulgated in the State Gazette No. 40 of 30 April 2013; Amended, SG 66 of 8 August 2014* Available from: http://www.ncpr.bg/images/News/Naredba_tseni_NCPR_eng.pdf.

19. Z. Mitkova, M. Manova, G. Petrova Relationship between generic competition and generic utilization of cardiovascular medicines monoproducts in Bulgaria. PHARMACIA, 2016; (LXIII)4: 3-14.