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Impact of reimbursement program “Affordable Medicines” on consumption of beta-blockers in Ukraine in 2017-2020

Gonchar Anton¹, Sholoiko Natalia²

¹ Ph.D. student, Department of Economy and Organization of Pharmacy, Bogomolets National Medical University, Kyiv, Ukraine.

² Candidate of pharmaceutical sciences, Associate Professor of the Department of Economy and Organization of Pharmacy, Bogomolets National Medical University, Kyiv, Ukraine.

Address for correspondence:

Gonchar Anton

E-mail: anton.a.gonchar@gmail.com

Abstract: *the article presents the results of the study of impact of the reimbursement program “Affordable medicines” on consumption of beta-blockers in Ukraine, used for treatment of cardiovascular diseases. Analysis was conducted based on analytical data of Ukrainian pharmaceutical market research system “PharmXplorer” of the company “Proxima Research”, with current legislation taken into account. It was estimated, that in 2021, according to international non-proprietary name and 5th level of ATC classification - two non-selective beta-blockers: propranolol (ATC code C07AA05) and sotalol (C07AA07); six selective beta-blockers: metoprolol (C07AB02), atenolol (C07AB03), betaxolol (C07AB05), bisoprolol (C07AB07), esmolol (C07AB09) and nebivolol (C07AB12); and one beta-blocker from alpha and beta blocking agents group – carvedilol (C07GA02) are allowed for medical use in Ukraine. From the beginning, when reimbursement program “Affordable medicines” was implemented (April 1st, 2017), only 4 beta-blockers were included in the reimbursement list. Consumption patterns were analyzed in terms of defined daily dose, and it was estimated that bisoprolol was the leader among all beta-blockers in terms of consumption in period from 2016 to 2020. The findings show, that among beta-blockers, that were included in the reimbursement list, the major annual growth of consumption was detected for bisoprolol and carvedilol, although the growth of consumption of metoprolol and atenolol was noted only within the first year of functioning of the reimbursement program “Affordable medicines”, and beginning from 2018, the consumption of these two beta-blockers was declining annually. Among beta-blockers, that were not included in the reimbursement list, the increase in annual growth of consumption was spotted for nebivolol and sotalol. DDD/1000 inhabitants/day indicators were calculated for each beta-blocker. It was found, that throughout the years the biggest value of this indicator was for bisoprolol – 8,46 in 2016; 11,74 in 2017; 15,28 in 2018 ; 16,88 and 17,48 in 2019 and in 2020 respectfully. The growth of this indicator can give evidence about positive effect of the reimbursement program “Affordable medicines” on consumption of bisoprolol and its affordability for population in Ukraine in 2017-2020.*

Key words: cardiovascular agents, drug utilization, pharmacoepidemiology, incentive.

Introduction

It was determined that cardiovascular diseases (CVD) are the main cause of death and disability worldwide. In 1990, the concept of Global Bur-

den of Disease (GBD) was introduced with the aim to give a worldwide view on human health, and 2020 published GBD data points out that disability became the major burden on the glob-

al health care system: in 1990 disability was accountable for 21% of total burden of diseases, and in 2019 it was accountable for more than a third (34%) of overall burden of diseases. (Murray et al., 2019) CVDs are currently increasing worldwide, and the number of deaths, caused by CVD, has increased up to 18,6 million in 2019, and have doubled the global disability, measured by DALYs and YYLs trends (Roth et al., 2020).

CVD are chronic, and in most cases, require a long-term treatment and consumption of medicines. (Husain et al., 2020) A lot of medicines are still not affordable to many patients due to high prices, especially to the lowest-paid workers. (Zaputko et al., 2017) (Sarayani, Rashidian & Gholami, 2014). In Europe, expenditures for CVD are estimated to be around 210 billion Euro annually. (Mitkova & Petrova, 2021) Chronic disease treatment requires a steady long-term consumption of two or more medicinal drugs, and as a result – may increase the cost of treatment. This issue can have an impact on affordability and medication adherence. (Curtler et al., 2017) Therefore, many countries worldwide implement reimbursement programs for CVD treatment, because high cost of medicines creates a risk of poor affordability of medicines for patients, and as a consequence, has a negative impact on public health. (Vogler et al., 2018)

Beta-blockers are widely used in family practice medicine to manage a variety of chronic cardiovascular conditions, such as hypertension and heart failure. (Fekadu et al., 2020) In arterial hypertension treatment, beta-blockers are considered at any point of treatment, if the patient has a specific indication for their use, such as heart failure, angina pectoris, atrial fibrillation and others. (Visseren et al., 2021)

Since April 1st 2017, a state government program “Affordable medicines” is functioning in Ukraine (Huz, Zaliska & Maksymovych, 2020), which provides a full or partial reimbursement of the costs for medicines for CVD treatment according to the approved list, which includes the following beta-blockers (BB): bisoprolol, metoprolol, atenolol, carvedilol (Piniashko, Zaliska & Ilyk, 2018). It was estimated that 7.2 million patients with cardiovascular diseases benefited from the program in 2017, despite its recent implementation. (Olga, G., Babar, Z. U. D., 2020). On the 1st of

April 2019, National Health Service of Ukraine, which is managing the program, has implemented the e-prescription into the program. (Zaliska, Huz, & Maksymovych, 2020).

Analysis of changes in consumption patterns, which arise under the influence of reimbursement programs can be considered as one of the indicators of increased affordability of medicines for the population and can be used to evaluate the effectiveness of such programs.

Aim

Study the impact of reimbursement program “Affordable medicines” on consumption of beta-blockers in Ukraine in period of 2017-2020.

To achieve the aim of the study, the following stages were planned:

I – To determine the list of beta-blockers, according to the international non-proprietary name (INN) and the 5th level of ATC classification, which are allowed for medical use in Ukraine.

II – Determine the consumption patterns of beta-blockers in Ukraine, in defined daily dose (DDD) terms, in period from 2016 to 2020.

III – To study the impact of the reimbursement program on consumption of beta-blockers in Ukraine, based on the analysis of calculations of indicators of annual growth of consumption in DDD terms, and indicators of DDD/1000 inhabitants/day for each beta-blocker in period from 2017 to 2020.

Materials and methods

The objects of the study were the regulatory framework governing the circulation, use and reimbursement of medicines in Ukraine, ATC Index guidebook, analytical data of Ukrainian pharmaceutical market research system “PharmXplorer” of the company “Proxima Research”. (Proxima Research, 2021) The methods of content analysis, comparative and logical analysis were used in this study.

Results and discussion

Current data of the State register of medicines of Ukraine (State expert center of Ukraine, 2021) shows that according to INN and the 5th level of ATC classification - two non-selective beta-blockers: propanolol (ATC code C07AA05) and sotolol (C07AA07); six selective beta-blockers: metoprolol (C07AB02), atenolol (C07AB03), betaxolol (C07AB05), bisoprolol (C07AB07), esmolol (C07AB09) and nebivolol (C07AB12); and one beta-blocker from the alpha and beta

INN	DDD mg	Consumed DDDs per year				
		2016	2017	2018	2019	2020
Propranolol	160	6 077 187	5 930 414	5 454 754	5 757 274	5 127 106
Sotalol	160	1 638 341	2 108 209	2 163 883	2 533 010	2 869 947
Metoprolol	150	15 086 012	17 172 559	16 340 061	16 275 448	15 507 643
Atenolol	75	6 645 745	7 685 150	7 371 259	6 735 767	5 786 288
Betaxolol	20	5 047 133	5 485 409	5 127 733	5 152 820	4 827 622
Bisoprolol	10	107 745 486	160 322 632	192 410 698	211 277 974	217 455 876
Nebivolol	5	30 297 855	37 305 766	40 070 993	45 722 034	49 555 353
Carvedilol	37,5	14 209 728	21 552 204	29 042 947	34 317 374	36 697 503

Table.1. Consumption patterns of beta-blockers in Ukraine in 2016-2020, in DDD terms.

blocking agents group – carvedilol (C07GA02) are allowed for medical use in Ukraine.

Analytical retail sales data, provided by Ukrainian pharmaceutical market research system “PharmXplorer” of the company “Proxima Research” was used to determine the consumption patterns of beta-blockers in Ukraine, except temporarily occupied territories of Crimea, Luhansk and Donetsk regions. Consumption patterns were measured in DDD terms, which is in line with WHO Collaboration Centre of Drug statistics guidelines, for each beta-blocker in period from 2016 to 2020. The analysis included only beta-blockers with oral route of administration.

Esmolol was excluded from the study due to its parenteral route of administration. The consumption patterns of beta-blockers in Ukraine in 2016-2020, in DDD terms, are presented in table 1.

Using the data from table 1, indicators of annual growth of consumption in DDD terms, for each beta-blocker were calculated. Results of calculations are presented in table 2.

Analysis of the data from table 2 shows, that since 2017, among beta-blockers, that were included in the reimbursement list, there was a significant increase of consumption of bisoprolol and carvedilol, and their consumption was growing throughout the period of 2018-2020. Data from ta-

Table 2.

Annual growth of consumption of beta-blockers in Ukraine, in DDD terms, in period 2017-2020.

№	INN	Annual growth of consumption per year, in DDDs, and in %.			
		2017	2018	2019	2020
1	Propranolol	-146 773 (-2,47%)	-475 660 (-8,72%)	302 519 (+5,25%)	-630 167 (-12,29%)
2	Sotalol	469 868 (22,29%)	55 675 (2,57%)	369 127 (14,57%)	336 937 (11,74%)
3	Metoprolol	2 086 547 (12,15%)	-832 498 (-5,09%)	-64 613 (-0,40%)	-767 806 (-4,95%)
4	Atenolol	1 039 405 (13,52%)	-313 891 (4,26%)	-635 492 (-9,43%)	-949 480 (-16,41%)
5	Betaxolol	438 276 (7,99%)	-357 677 (-6,98%)	25 087 (0,49%)	-325 197 (-6,74%)
6	Bisoprolol	52 577 146 (32,79%)	32 088 066 (16,68%)	18 867 276 (8,93%)	6 177 902 (2,84%)
7	Nebivolol	7 007 910 (18,79%)	2 765 227 (6,90%)	5 651 041 (12,36%)	38 33 319 (7,74%)
8	Carvedilol	7 342 476 (34,07%)	7 490 743 (25,79%)	5 274 427 (15,37%)	2 380 129 (6,49%)

ble 2 also indicates a decrease in consumption of metoprolol and atenolol in period of 2018-2020, despite the fact, that these beta-blockers were also included in the reimbursement list in Ukraine. Among the beta-blockers, that were not included in the reimbursement list in Ukraine, a growth of consumption of nebivolol and sotalol was observed in 2017-2020, and consumption of propranolol was decreasing, except the period of year 2019. Consumption of betaxolol increased only in 2017, but throughout the period of 2018-2020 the consumption had a general decreasing trend.

Guidelines for ATC classification and DDD assignment (*WHO, 2021*) estimate, that the indicator DDD/1000 inhabitants/day is useful in drug utilization research for medicines, which are used to treat chronic medical conditions, like CVD. Given the fact, that this study analyses the medicines, that are used to treat adults, the calculation of indicators DDD/1000 inhabitants/day was based on official data of adult population in Ukraine. According to the State Statistics Center of Ukraine (*Державна служба статистики України, 2022*), the adult population of Ukraine in 2016 was 34 888 086 people, in 2017 – 34 703 383, in 2018 – 34 505 664, and in 2019 and 2020 – 34 301 355 and 34 078 945 adults respectfully. Using this data, the calculations of DDD/1000 inhabitant/day indicators for each beta-blocker were performed. The results of calculations are presented in table 3.

Analysis of the results of calculations shows, that among beta-blockers, that were included in the reimbursement list, the positive dynamic of indicators was among bisoprolol and carvedilol, and indicators of metoprolol and atenolol had insignificant changes. Among beta-blockers that were not included in the reimbursement list, the indicators of DDD/1000 inhabitant/day were growing for nebivolol, and to a lesser extent, for sotalol, but indicators for propranolol and betaxolol had minor changes, which indicates a stable adherence among patients to these medicines, considering their effectiveness and safety.

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Conclusions

Reimbursement program “Affordable medicines” had a positive impact on consumption of beta-blockers in period from 2017 to 2020 in Ukraine, mostly of bisoprolol and carvedilol, by increasing their affordability. It is also worth noting, that the reimbursement program did not have a negative impact on consumption of beta-blockers, that were not included in the reimbursement list, and did not cause a redistribution of consumption of beta-blockers, that could be influenced by the patient’s refusal to consume beta-blockers, that are not reimbursed, and make a switch to consume beta-blockers, that are included in the reimbursement list. This indicates the need to update and include other beta-blockers the reimbursement list in Ukraine, which is supported by the data of their stable use among patients.

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This study did not obtain any external funding or financial support.

Conflict of interests

Authors have no conflict of interest to declare.

Consent to publication

All authors have read and approved the final version of this manuscript. All authors agreed to publish this manuscript.

Table 3.

DDD/1000 inhabitants/day indicators for beta-blocker in Ukraine in period from 2016 till 2020.

№	INN	2016	2017	2018	2019	2020
1	Propranolol	0,48	0,43	0,43	0,46	0,41
2	Sotalol	0,13	0,15	0,17	0,20	0,23
3	Metoprolol	1,18	1,26	1,30	1,30	1,25
4	Atenolol	0,52	0,56	0,59	0,54	0,47
5	Betaxolol	0,40	0,40	0,41	0,41	0,39
6	Bisoprolol	8,46	11,74	15,28	16,88	17,48
7	Nebivolol	2,38	2,73	3,18	3,65	3,98
8	Carvedilol	1,12	1,58	2,31	2,74	2,95

ORCID ID and Authors contribution [0000-0002-5083-7218](https://orcid.org/0000-0002-5083-7218) (A,D,E,F) Sholoiko
[0000-0002-2088-0645](https://orcid.org/0000-0002-2088-0645) (A,B,C,D) Gonchar Natalia
Anton

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Вплив програми реімбурсації «доступні ліки» на споживання лікарських засобів класу бета-блокаторів в Україні в 2017-2020 роках

Гончар Антон¹, Шолойко Наталія²

¹ Аспірант кафедри організації та економіки фармації, Національного медичного університету імені О.О. Богомольця, м. Київ, Україна

² Канд.фарм.наук, доцент кафедри організації та економіки фармації, Національного медичного університету імені О.О. Богомольця, м. Київ, Україна

Address for correspondence:

Gonchar Anton

E-mail: anton.a.gonchar@gmail.com

Анотація: в статті представлено результати дослідження впливу програми відшкодування вартості лікарських засобів «Доступні ліки» в Україні, на споживання лікарських засобів класу бета-блокаторів для лікування серцево-судинних захворювань. Аналіз проводився на основі аналітичної системи дослідження фармацевтичного ринку України «PharmXplorer» компанії «Проксіма Рісерч» з урахуванням чинної нормативно-правової бази. Встановлено, що у 2021 році в Україні дозволено до медичного застосування (zareєстровано) за міжнародною непатентованою назвою (МНН) 2 неселективних бета-блокатори, 6 селективних бета-блокаторів та 1 бета-блокатор класу блокаторів α - і β -адренорецепторів. З початку дії державної програми «Доступні ліки» (квітень 2017 року) до переліку лікарських засобів, що підлягають відшкодуванню було включено лише 4 бета-блокатори. Аналіз структури споживання проводився за показником добової дози лікарського засобу (defined daily dose, DDD) та було встановлено, що лікарські засоби бісопрололу були лідером в споживанні серед всіх бета-блокаторів в період з 2016 по 2020 роки. Виявлено, що серед бета-блокаторів, вартість яких підлягали відшкодуванню, відзначався значний щорічний приріст у споживанні бісопрололу та карведилолу, а збільшення використання препаратів на основі метопрололу та атенололу відзначалось лише в перший рік функціонування програми «Доступні ліки», та починаючи з 2018 року відбувалось подальше щорічне зниженням споживання цієї групи бета-блокаторів. Серед бета-блокаторів, вартість яких не підлягала відшкодуванню, збільшення щорічного приросту споживання відмічалось лише у препаратів небіволулу та соталолу. Було розраховано показник DDD/1000 мешканців/на день. Виявилось, що найбільшим цим показником протягом всіх років був у препаратів бісопрололу – 8,46 в 2016 році; 11,74 в 2017; 15,28 в 2018 ; 16,88 та 17,48 в 2019 та 2020 роках відповідно. Зростання цього показника може свідчити про позитивний вплив програми «Доступні ліки» на споживання препаратів бісопрололу та їх доступність для населення України в 2017-2020 роках.

Ключові слова: бета-блокатор, серцево-судинні препарати, споживання ліків, фармакоепідеміологія, реімбурсація, стимулювання.



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