

NAUKI FARMACEUTYCZNE: EDUKACJA, EKONOMIKA I ZARZĄDZANIE

Doctor of pharmacy, professor Tolochko V. M.

PhD (Pharmacy), assistant professor Adonkina V. Iu.

National University of Pharmacy

+38(057)7327558

uef-ipksf@ukr.net

DIURETICS: STUDY OF ASSORTMENT, SOCIAL AND ECONOMIC AFFORDABILITY AND CONSUMPTION IN UKRAINE

ŚRODKI MOCZOPĘDNE: BADANIE ASORTYMENTU, ASORTYMENTU, DOSTĘPNOŚCI SPOŁECZNO- EKONOMICZNEJ ORAZ POZIOMU SPOŻYCIA NA UKRAINIE

Tolochko V. M., Adonkina V.

Iu. Diuretics: Study of Assortment, Social and Economic Affordability and Consumption in Ukraine.

The article deals with the results of analysis of the diuretics pharmaceutical market, assessment of their social and economic affordability and consumption in Ukraine. It has been established that during 2009 - 2015 there were some changes in the assortment of diuretics - the number of domestic drugs increased. The vast majority of the drugs are affordable for an average Ukrainian citizen; this fact provides the ability to select the drug considering its cost, efficiency and safety. The consumption of diuretics has increased for the period under the study. The use of loop diuretics is higher, because their diuretic effects are more pronounced than the effects of thiazides, thiazide-like diuretics and potassium-sparing diuretics.

Keywords: arterial hypertension (AH), diuretics, social and economic affordability,

indicator of payment adequacy, consumption, ATC/DDD-methodology.

Tolochko W.M., Adonkina W.J. Środki moczopędne: badanie asortymentu, asortymentu, dostępności społeczno-ekonomicznej oraz poziomu spożycia na Ukrainie. W artykule zaprezentowano wyniki analizy rynku farmaceutycznego środków moczopędnych, oceny ich dostępności społeczno-ekonomicznej oraz poziomu spożycia na Ukrainie. Ustalono, iż w latach 2009-2015 miały miejsce zmiany w asortymencie diuretyków – zwiększyła się ilość krajowych środków lekarskich. Zdecydowana większość preparatów jest bardzo dostępna dla statystycznego mieszkańca Ukrainy, co umożliwia wybór środka lekarskiego z uwzględnieniem jego wartości, efektywności i bezpieczeństwa. W badanym okresie zwiększył się poziom spożycia diuretyków. Przeważa spożycie diuretyków pętlowych, efekt moczopędnych jest wyraźniejszy, niż w przypadku tiazydowych, tiazydopodobnych i oszczędzających wapń.

Słowa kluczowe: nadciśnienie tętnicze, diuretyki, dostępność społeczno-ekonomiczna, współczynnik adekwatności wypłacalności, spożycie, metodologia ATC/DDD

Problem statement. Arterial hypertension (AH) is one of the most problematic diseases of people around the world clinically and economically. This occurs because the vascular disorders caused by AH, affect mainly able-bodied population. They cause the damage of target organs: heart, brain, retina, kidneys and arteries; and they cause such dangerous complications of AH as myocardial infarction and stroke. Thus, AH leads to serious social and economic consequences caused by high morbidity and mortality. In this regard, medical professionals understand that drug and non-drug preventive measures to avoid AH complications should be routine practice for patients with high blood pressure (BP) [5].

One of the classes of the first-line antihypertensive drugs (AHD) is diuretics, particularly thiazides and thiazide-like diuretics. They have been used to treat AH since 1957, when the first drug of this group

was synthesized - Chlorothiazide [2]. Apart from convincingly proven ability to reduce blood pressure and cardiovascular complications of AH diuretics have several additional advantages versus other first-line AHD: low cost, there is no “withdrawal syndrome”, efficiency in single dose, strengthening of other AHD action as combined use; that allows using them for pharmacotherapy of most patients with AH.

The most important motivation for patients to treat AH regularly is the efficacy and safety of treatment (minimum of side effects) and social and economic affordability of the drugs, which depends on the price. The last factor for Ukrainian patients is often the determining factor, because the patient is the primary payer of pharmacotherapy funds.

Analysis of recent researches and publications. Nowadays in the scientific literature there are publications [5, 6], which represent the consumption of certain drugs in Ukraine, including AHD, results of the analysis of their social and economic affordability and assortment. These publications do not include references to the results of the relation analysis between the assortment, affordability and consumption of diuretics as first-line drugs for the treatment of AH.

Taking into account the abovementioned, the purpose of this work was to study the assortment, social and economic affordability and consumption of diuretics in the Ukrainian pharmaceutical market. To achieve this purpose it was necessary to solve the following issues: to analyse the assortment of diuretics at the beginning of 2016; to conduct a study of the social and economic affordability and to explore the dynamics of consumption of diuretics in the pharmaceutical market of Ukraine during 2008-2015.

Basic material statement. Analysis of diuretics assortment, their social and economic affordability and consumption was carried out during 2008-2015 according to the information of “Morion” retrieval system about assortment, price, number of the sold packages of drugs for a certain year. An

indicator of payment adequacy ($C_{a.s.}$) was calculated to analyse social and economic affordability of diuretics. The indicator shows the share of the salary spent on one package of the drug [4, 6]. Analysis of the consumption of diuretics was carried out using ATC/DDD-methodology [3]. Consumption of drugs was evaluated as index DDDs/1000 inhabitants /day (DIDs), which was calculated by the formula: $DIDs = DDDs \times 1000 / \text{number of inhabitants} \times 365$, where DDDs are the defined daily doses (DDD), which were taken by patients in Ukraine for the certain year. Figures of DDD of the analysed drugs were taken at WHO (www.whocc.no/atc_ddd_index/) according to the corresponding ATC code.

Diuretics have different chemical structure; they are different in mechanism, localization, strength, speed, duration of action and possible adverse reactions [1].

There are following groups of diuretics according to the existing classification:

- thiazide (Hypothiazid) and thiazide-like (Chlorthalidone, Indapamide, Xipamide) diuretics, which are active on the cortical segment of the loop of Henle and detect moderate diuretic effect. These drugs are the most important for long-term treatment of AH;
- loop diuretics (Furosemide, Ethacrynic Acid, Torasemide), which are active throughout the loop of Henle and detect the strongest diuretic effect, and they are essential in the pharmacotherapy of emergency conditions: hypertensive crisis, cerebral edema, at treatment of AH combined with chronic heart failure and post-infarction cardiosclerosis;
- potassium-sparing diuretics: competitive aldosterone antagonists (Spironolactone, Eplerenone) and non-competitive aldosterone antagonists (Triamterene, Amiloride), which are active at the level of the distal tubules of nephron and detect weak diuretic effect;
- diuretic combination drugs (Triamterene + Hypothiazid, Amiloride + Hypothiazid, Spironolactone + Furosemide) detect

stronger diuretic effect compared to the mono-drugs.

Thiazide and thiazide-like diuretics are the most important for long-term treatment of AH; they detect moderate diuretic effect and meet the requirements of safe long-term treatment.

Diuretics were presented in Ukrainian pharmaceutical market on January 1, 2016 as 11 INN; among them there were 8 INN – mono-drugs and 3 INN – combination of Hydrochlorothiazide and loop diuretics: Triamterene and Amiloride and combination of potassium-sparing and loop diuretics: Spironolactone + Furosemide.

Diuretic assortment consisted of 48 TNs (trade names), which were presented by 87 drugs of different dosage forms (tablets and capsules) and dosages. The largest number of TNs, i.e. 41.6%, was presented by high-active loop diuretics: sulfonamides, mainly due to Torasemide (12 TNs), and the lowest number, i.e. 2.1%, - by derivatives of arylacetic acid (by Ethacrynic Acid).

During the period under study it was found out that the share of foreign drugs was the biggest - 65-76.3% of the available diuretics assortment in the market, and the share of domestic drugs was 23.7-35%. Thus, foreign drugs prevail over domestic in the market (Figure 1).

Figure 1. Dynamics of the structure of diuretics assortment during 2009-2015

The analysis of the dynamics of the structure of diuretics assortment during the period under study has shown that they tend to increase. In 2010 the number of foreign drugs increased on average by 45% in comparison with 2009, and the number of domestic drugs remained the same. In 2015 foreign diuretics assortment decreased by 7% in comparison with 2012, i.e. by 4 drugs considering the dosage forms. Number of domestic drugs increased from 18 in 2009 to 30 in 2015, their share also increased, it was equal to 31% and 35.5% of the total diuretics assortment.

34 pharmaceutical manufacturers,

including 24 foreign ones and 10 domestic ones, supply the diuretics to the market. The leaders of manufacturing companies according to the number of manufactured TNs of diuretics are the following: “Sandoz” (Switzerland), “Farmak” JSC (Ukraine, Kyiv), “Berlin-Chemie/Menarini Group” (Germany). Ukraine takes first place in the general ranking of manufacturers according to the number of diuretics (which is 27 drugs).

The results of the evaluation of economic affordability of diuretics of different pharmacological subgroups, which was carried out according to the indicator of payment adequacy ($C_{a.s.}$), are set out in the Table.

Evident dependence of social and economic affordability on pharmacotherapeutic subgroup of diuretics was established. During the period under study most diuretics were high affordable. All TNs of thiazides, thiazide-like diuretics and fixed combinations of diuretics (100% TNs), which are the most important in the treatment of AH, were high affordable for Ukrainian patients. Significant share (average 85.9%) of TNs in the group of loop diuretics was high affordable for consumers throughout the period under study. The largest share of low affordable drugs (33% -13.3%) is specific to potassium-sparing diuretics, i.e. these drugs are the most unaffordable for consumers, but during the last three years the share of average affordable drugs in this group increased (from 20% to 46.7%).

Consequently, conducted analysis of diuretics assortment for the period 2009-2015 has shown that most drugs are foreign. The most affordable diuretics for an average citizen of Ukraine are thiazides, thiazide-like diuretics and fixed combinations of diuretics, which are used to treat AH more often than other drugs.

Table

Classification of diuretics by different categories of economic affordability according to the indicator of payment adequacy

Subgroups of diuretics	Drug category	Years under study						
		2009	2010	2011	2012	2013	2014	2015
		% of drugs						
Thiazide and thiazide-like diuretics: Hypothiazid, Indapamide, Xipamide	high affordable, Ca.s.<5%	100	100	100	100	100	100	100
	average affordable, 5% <Ca.s.<15%	—	—	—	—	—	—	—
	low affordable, Ca.s.>15%	—	—	—	—	—	—	—
Loop diuretics: Furosemide, Torsemide	high affordable, Ca.s.<5%	100	85,7	86,3	88	85,7	85,1	70,8
	average affordable, 5% <Ca.s.<15%	—	9,5	7,8	8	12,3	10,6	25
	low affordable, Ca.s.>15%	—	4,8	5,9	4	2	4,3	4,2
Potassium-sparing diuretic (aldosterone antagonists): Spironolactone, Eplerenone	high affordable, Ca.s.<5%	67	67	67	75	60	50	40
	average affordable, 5% <Ca.s.<15%	—	—	—	—	20	33,3	46,7
	low affordable, Ca.s.>15%	33	33	33	25	20	16,7	13,3
Fixed combinations: Triamterene + Hypothiazid, Acetazolide + Hypothiazid	high affordable, Ca.s.<5%	100	100	100	100	100	100	100
	average affordable, 5% <Ca.s.<15%	—	—	—	—	—	—	—
	low affordable, Ca.s.>15%	—	—	—	—	—	—	—

The analysis of diuretics consumption by DIDs index has shown that there were some changes during the period under study: increase (8.28-9.77 DIDs) of the consumption in 2008-2013, and gradual decrease (8.91 DIDs) in 2015. Study of intra-group structure of diuretics consumption (Figure 2) has shown that almost 50-52% of the total consumption is the share of loop diuretic - Furosemide (4.69-4.60 DIDs). The consumption share of a new loop diuretic Torasemide is only 5-12.2% of the total consumption of diuretics (0.44-1.09 DIDs).

Consequently, loop diuretics are the largest consumption group; they are essential in the pharmacotherapy of emergency conditions. Consumption of thiazides and thiazide-like diuretics, which are the first-line drugs for the treatment of AH, are the second after the loop diuretics and are significant in comparison with other drugs.

Conclusions. For the period 2009-2015 under study there were changes in the assortment of diuretics, which were represented in the pharmaceutical market of Ukraine. The number of domestic drugs increased, and the number of foreign drugs decreased. This fact is considered to be positive as domestic drugs are more affordable for patients.

Analysis of the economic affordability of diuretics has shown that most drugs are high affordable for an average Ukrainian citizen, that makes possible to choose drugs considering their efficacy, safety and cost. A significant proportion of potassium-sparing diuretics and new generation loop diuretics due to their high price are economically unaffordable for the vast majority of Ukrainians, especially for disadvantaged population. Therefore the introduction of a system of reimbursement (partial or full) of the drugs cost to patients is required.

During 2008-2015 the consumption of diuretics increased. More effective drugs are more consumed – loop diuretics, their diuretic effects are more pronounced than the effects of thiazides, thiazide-like diuretics and potassium-sparing diuretics, they are often used in emergency conditions. Consumption

of thiazides and thiazide-like diuretics, which are the first-line drugs, are the second after the loop diuretics.

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