COMPARATIVE ANALYSIS OF DRUG CONSUMPTION FOR THE TREATMENT OF EPILEPSY IN UKRAINE, KAZAKHSTAN AND BELARUS

Iuliia Korzh, Natalia Olieinikova, Marharyta Beketova, Inna Kubarieva, Yevheniia Korobova, Oleksandr Sevriukov, Olga Afanasenko

The aim to conduct a comparative analysis of the population’s consumption of antiepileptic drugs in the retail pharmaceutical markets of developing countries, including Ukraine, Kazakhstan and Belarus in the period 2016–2020.

Materials and methods. The objects of the research were the data of marketing agencies that monitor the domestic pharmaceutical market in the countries under study. In particular, the range of AED in Ukraine was determined using the market research system «Pharmstandard» of the company «Morion». Analytical-comparative, systematic, graphical, logical, mathematical-statistical research methods were used.

Results. The results of the study show that the market of antiepileptic drugs in Ukraine, Kazakhstan and Belarus mainly depends on foreign manufacturers, in particular by 60%, 92% and 46% respectively in 2020, and does not meet the needs of the population in accordance with WHO recommendations. It is established that in the market of Ukraine, Kazakhstan during 2016–2019 there is a general trend of increasing retail sales of antiepileptic drugs, which are not included in the WHO Basic List of Essential Medicines, both in natural and in monetary terms. The results of the analysis of retail sales of drugs in the Belarusian market in quantitative and monetary terms indicate an increase in sales of drugs for the treatment of epilepsy, which are included in the WHO Basic List of Essential Medicines.

Conclusions. The presence in Ukraine of a difficult situation with the consumption of antiepileptic drugs in comparison with other countries of the reference group indicates the need to implement comprehensive programs to combat the spread of epilepsy and the introduction of models for the rational use of limited health resources.

Keywords: pharmaceutical market, consumption volumes, epilepsy, antiepileptic drugs, growth/loss rates, WHO Basic List of Essential Medicines

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1. Introduction

In any country, the issue of providing affordable medical and pharmaceutical care to the population appears as one of the most important areas of public policy in accordance with the objectives of the National Medical Policy [1]. Increasing the availability of medicines used in the treatment of socially significant pathologies remains a priority issue of public health policy in developing countries. Given the growing tendencies to increase society’s demands for efficiency of services provided in the health care system, as well as given the significant gap in the levels of availability of these services for different social groups, the role of the state in financing this industry is constantly transformed [2–4]. In Ukraine, the reform of the pharmaceutical sector in healthcare system has been identified as one of the main areas of state policy aimed for developing of effective mechanisms for providing population, and in developing countries, this figure is twice as high [5]. According to population-based research conducted in developed countries, the incidence of epilepsy ranges from 0.28 to 0.53 per 1,000 population. In developing countries, the prevalence of epilepsy varies widely, from 3.6 per 1,000 people in India to 40 per 1,000 people in rural Nigeria. In the CIS countries, the prevalence of epilepsy ranges from 0.96 to 10 per 1,000 population. In Europe, 6 million people suffer from epilepsy, 40% of whom do not receive adequate treatment, while in middle and low living countries the share of such patients is 50% and 75%, respectively [6, 7].

The above-mentioned problem of increasing the prevalence of epilepsy among the population, limited public funding for health care in many countries and the rapid development of the global pharmaceutical market indicate the need for rational choice of drugs [8]. Establishing leading drugs in terms of sales in each segment of the drug market, comparing data with the structure of disease prevalence, standard treatments, and evidence-based medicine on the effectiveness of drugs provide an opportunity to assess the rationality of a particular drug in a particular nosology.
The aim to conduct a comparative analysis of the population’s consumption of antiepileptic drugs in the retail pharmaceutical markets of developing countries, including Ukraine, Kazakhstan, and Belarus in the period 2016–2020.

2. Planning (methodology) of the research
To achieve this goal, the following stages of the study are planned:

I stage – analysis of the dynamics of indicators of growth/loss of retail sales of AED by pharmacotherapeutic groups in the pharmaceutical markets of Ukraine, Kazakhstan, Belarus in physical and monetary terms for the period 2016–2020;

II stage – analysis of the dynamics of AED sales in terms of domestic and foreign, taking into account the growth rates of their sales in the pharmaceutical markets of Ukraine, Kazakhstan, Belarus in kind and in monetary terms for the period 2016–2020;

III stage – study of retail sales of drugs for the treatment of epilepsy, which are listed in the WHO Basic List of Essential Medicines and AED not included in it, considering the growth rate of their sales in kind and cash equivalents.

3. Materials and methods

The pharmaceutical markets of Ukraine, Kazakhstan and Belarus were selected as the subject of the study in the period 2016–2020. Countries for the study were determined by us based on similar indicators characterizing the level of socio-economic development of states, namely the characteristics of economic models of health and sources of funding, the level of budget expenditures on health in relation to gross domestic product, solvency [9]. Thus, the main criterion used in the formation of the countries of comparison was the similarity with Ukraine in historical, political, socio-economic and other parameters of state development. According to this set of parameters, the most identical to the Ukrainian realities, in our opinion, were Belarus and Kazakhstan.

The objects of the research were the data of marketing agencies that monitor the domestic pharmaceutical market in the countries under study. In particular, the range of AED in Ukraine was determined using the market research system “Pharmstandard” of the company “Morion” [10].

Retail sales growth rates were calculated in monetary and natural terms (in terms of sales in US dollars) and (by number of packages sold). The analysis of the dynamics of changes by years and from the selected indicative years was implemented with using growth rates (%) and growth rates (%). The calculations were performed according to the following formula:

\[ \text{RSGrate} = \left( \frac{S_n - S_{n-1}}{S_{n-1}} \right) \times 100 \% \],

where RSG rate – retail sales growth rate (%);

\( S_n \) – indicator of retail sales of drugs for the treatment of epilepsy in natural and monetary terms for the year.

Structural analysis of the studied segment of the pharmaceutical market was performed according to the V level of ATC classification, in accordance with the WHO recommendations on the analysis of drug consumption and in marketing research in general [11]. Statistical data processing was performed using the statistical analysis package Statistica (version 12.0, StatSoft, Tulsa, USA). A \( p \)-value<0.05 was considered statistically significant.

4. Research results

Priority factors that influence the formation of the pharmaceutical market of any country, determine its dynamics and structural changes, are trends in the demographic situation; dynamics of budget funding for health development; availability and implementation of national and international health programs; trends in the weighted average cost of packaging of drugs in terms of domestic and foreign manufacturers; the level of solvency of the population and the impact of the inflation component on the sales of drugs; trends in the development of sales of drugs by groups [12].

According to the results of the study, it was found that the AED market of Ukraine, Kazakhstan and Belarus mainly depends on foreign producers, including 60 %, 92 % and 46 % respectively in 2020, and does not meet the needs of the population in medicines according to WHO recommendations (Fig. 1, 3, 5). Also noteworthy is the small share of domestic products in terms of value in the AED market, which is about 22 % for Ukraine, 5 % for Kazakhstan and 31 % for Belarus (Fig. 2, 4, 6). This trend, in our opinion, is due to the fact that domestic industry is focused on the production of a range of drugs of the lower price segment.

The analysis of sales of drugs in the pharmaceutical market of Ukraine in physical terms shows that during 2016–2019 there is a general trend of growth in retail sales of AED. However, it was found that the above indicator is characterized by an annual decrease in the range of growth (RSG rate 2017=21.07 %, RSG rate 2018=18.56 %, RSG rate 2019=4.74 %) (Table 1). This situation is due to the fact that in 2017 there was a decrease in sales in natural terms only for 2 INN, benzobarbital (RSG rate 2017=–0.83 %; RSG rate 2018=–4.18 %; RSG rate 2019=–10.43 %) and phenytoin (RSG rate 2017=–6.97 %; RSG rate 2018=–8.26 %; RSG rate 2019=–2.70 %), in 2018, gabapentin joined the mentioned INN AED (RSG rate 2018=–0.96 %; RSG rate 2019=–13.41 %), 2019 – phenobarbital (RSG rate 2019=–1.58 %) carbamazepin (RSG rate 2019=–7.90 %).

Pregabalin were the leaders in terms of growth rates in terms of sales of AED packages in 2017 (RSG rate 2017=133.24 %, 2018 and 2019 – lacosamide (RSG rate 2018=837.47 %; RSG rate 2019=224.76 %), and in 2020 – levetiracetam (RSG rate 2020=22.67 %).

According to the study, in 2020 there was a general negative trend to reduce retail sales of AED in natural terms (RSG rate 2020=–3.87 %), which arise even in the emergence of a new subgroup of AED in the pharmaceutical market, namely – zonisamide, sales in 2020 amounted to 1159 packages. The established fact is of concern and requires further research, as the importance of epilepsy among the population of Ukraine is growing (the
total number of epilepsy patients increased from 51,153 in 2016 to 52,482 people in 2018) [13, 14], and the number of sold packages of drugs rapidly decreasing.

The results of the study of sales of the AED market of Kazakhstan (Table 1) in physical terms allowed to establish the opposite trend in Ukraine. During 2016-2019 there was a gradual decrease in sales of drugs in the studied segment, as evidenced by the data obtained: RSG rate 2017=-1.69; RSG rate 2018=-10.71; RSG rate 2019=-6.77. Thus, the significant decrease in AED growth rates in 2017 compared to 2016 is primarily due to the disappearance from the retail pharmaceutical market of Kazakhstan of some drugs of the barbiturate group and their derivatives (RSG rate 2017=-100 %) and reducing the number of packages of phenobarbital subgroups sold (RSG rate 2017=-32.70 %) klonazepam (RSG rate 2017=-37.86 %). The decrease in sales in packaging was mainly due to a decrease in sales of valproic acid (RSG rate 2018 = –38.23 %) topiramate (RSG rate 2018=–91.42 %), and 19 -aminobutyric acid (RSG rate 2019=–39.07 %) and topiramate (RSG rate 2019=–73.72 %).

In 2020, the pharmaceutical market of Kazakhstan has a general trend of growth in retail sales of AED in the natural terms (RSG rate 2020=5.24 %). The highest value of the rate of growth was recorded among such drugs for INN as: topiramate (RSG rate 2020=95.29 %) and pregabalin (RSG rate 2020=34.81 %).

The results of the analysis of the pharmaceutical market of Belarus (Table 1) allowed us to establish that during 2016-2020 there is a stable positive trend of growth in sales of AED in physical units (RSG rate 2017=4.83 %; RSG rate 2018=10.81 %; RSG rate 2019=16.79 %; RSG rate 2020=11.23 %) with a characteristic annual growth during 2017–2019 of the range of values of the studied indicator.

Levetiracetam was identified as the leader among AEDs in the Belarusian market in terms of sales in packaging in 2017 (RSG rate=107.64 %), in 2018 and 2019 - oxcarbazepine (RSG rate 2018=1418.14 %; RSG rate 2019=1964.66 %) and pregabalin (RSG rate 2018=114.57 %; RSG rate 2019=128.41 %). In 2020, the largest growth rates were shown by the subgroups of vigabatrin, oxcarbazepine and levetiracetam, whose consumption increased compared to 2019 by 97.58 %, 88.20 % and 83.22 %, respectively.

A characteristic feature of the pharmaceutical market of Ukraine during 2017–2020 is the stable positive dynamics of AED sales in monetary terms (Tab. 2). The largest increase in sales of this market segment in monetary terms was recorded in 2018 and amounted to 32.96 %. The leaders among AED in terms of sales in monetary units each year during 2017–2019 were lacosamide, consumption of which increased by 88.45 % (in 2017), 866.32 % (in 2018) and 215.78 % (in 2019). In 2020, the largest increase in sales was observed clonazepam (RSG rate=30.38 %).

The data of the analysis of sales of AED in the market of Kazakhstan (Table 2) on a similar indicator showed its increase in 2017 compared to 2016 by 5.50 %. At the same time, in the period 2018–2020, significant negative shifts in the dynamics of drug sales were noted in relation to this market segment. Thus, the decrease in sales of drugs in monetary terms by 18.44 % is observed in 2018, by 3.55 % – 2019, by 4.04 % – 2020. It should be noted that the highest rates of loss in 2018 and 2019 were recorded in the AED subgroup of topiramate, and the subgroup of clonazepam – 2020.

The analysis of AED consumption in cash equivalent in the pharmaceutical market of Belarus (Table 2) showed a positive dynamic of growth during 2017–2020 and was 17.28 %. It should be noted that in 2017 the largest increase in consumption in monetary terms was provided by drugs of the levetiracetam subgroup, sales of which increased by 52.32 % compared to 2016. However, it should be noted that in 2017 in the pharmaceutical market of Belarus Oxcarbazepine subgroup appeared, which in the period 2018–2020 became the annual leaders among AED in terms of growth rate, as evidenced by the increase in sales in monetary terms by 1340.80 % in 2018, by 204.30 % in 2019 and by 95.11 % in 2020.

According to the next stage of the study, which provides an analysis of the growth rate of retail sales in terms of domestic and foreign production, in the pharmaceutical markets of Ukraine and Kazakhstan identified negative changes in the dynamics of sales of domestic AED in natural estimates.

It should be noted that in 2020 the number of sold packages of domestic AED on the market of Ukraine (Fig. 1) decreased by 12.86 % and 28.83 % on the market of Kazakhstan (Fig. 2).

The highest rates of domestic AED in Ukraine were shown by drugs of the subgroups carbamazepine (–24.60 %) and gabapentin (–22.85 %), in Kazakhstan – subgroups of lamotrigine (–75.23 %) and levetiracetam (–67.28 %). However, special attention is drawn to the fact that during the study period in the pharmaceutical markets of these countries some AED of domestic production, especially drugs of the subgroup of valproic acid, which according to international protocols are defined as first-line drugs for epilepsy in all types of seizures [15–18].

In the conditions of a significant decrease in the number of sold packages of domestic AED in 2019 in the market of Ukraine and Kazakhstan, there was the opposite trend to increase sales of these drugs in cash by 24.89 % and 1.47 %, respectively (Fig. 3, 4). At the same time, already in 2020, the growth rate was reduced by almost 5 % for Ukrainian-made drugs and by 28.83 % for Kazakhstan-made drugs.

According to the results of the study of the Ukrainian market, there is a constant trend during 2016–2020 of increasing the volume of retail sales of foreign-made AED in both quantitative and cost terms. It was also found that in monetary terms, the above indicator is characterized by a much larger range of growth than in quantitative terms, which indicates a significant increase in the cost of the studied drugs, and, consequently, reduces their availability to the population.

A characteristic feature of the pharmaceutical market of Kazakhstan is the negative dynamics of sales of foreign-made AED in monetary terms, which is monitored during 2018–2020 on the contrary, there is an increase in the studied indicator by 6.12 %.
Table 1

Dynamics of growth rates (GR) of retail sales of medicines for treatment of Epilepsy in natural terms for Ukraine, Kazakhstan and Belarus

<table>
<thead>
<tr>
<th>INN</th>
<th>ATC index</th>
<th>Ukraine GR, %</th>
<th>Kazakhstan GR, %</th>
<th>Belarus GR, %</th>
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Note: * – medicines which appeared on the pharmaceutical market only in 2020; ** – medicines which were present on the pharmaceutical market only until 2016 (inclusive)

Table 2

Dynamics of growth rates (GR) of retail sales of medicines for treatment of Epilepsy in cash for Ukraine, Kazakhstan and Belarus

<table>
<thead>
<tr>
<th>INN</th>
<th>ATC index</th>
<th>Ukraine GR, %</th>
<th>Kazakhstan GR, %</th>
<th>Belarus GR, %</th>
</tr>
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Note: * – medicines which appeared on the pharmaceutical market only in 2020; ** – medicines which were present on the pharmaceutical market only until 2016 (inclusive)
The above results of the study of the pharmaceutical markets of Ukraine and Kazakhstan indicate a decrease in the number of sales of domestic AED relative to foreign. At the same time, it was found that the largest volume of sales in monetary units is provided by foreign-made drugs, which in the Ukrainian market account for 80% of total sales of AED and in Kazakhstan – 95% in 2016–2020 mechanisms of import substitution of AED, which, in our opinion, will provide the population of these countries with efficient, high quality and affordable AED of domestic production.

The results of the analysis of the pharmaceutical market of Belarus in terms of retail sales of AED both domestic and foreign production in monetary and physical terms during 2016–2020 show a growth trend (Fig. 5, Fig. 6). Interesting, the greatest value of the indicator of the growth rate was recorded in 2019 and in physical terms is 20.00% for foreign and 14.23% for domestic AED, and in monetary terms – 15.49% (foreign AED) and 21.44% (domestic AED).

As you know, the most important guiding documents that help countries choose vital medical products that should be widely available and affordable at all levels of the health system, is developed by the WHO Basic List of Essential Medicines [19, 20]. Today, more than 150 countries around the world are guided by the List of Essential Medicines in making scientifically sound decisions about which drugs provide maximum cost-effectiveness in terms of impact on public health.

Based on the above, the next stage of the study was the analysis of retail sales of drugs for the treatment of epilepsy in kind, which are part of the WHO Basic List of Essential Medicines and AED, which are not in it.
Fig. 3. Dynamics of indicators of retail sales of antiepileptics in cash for the pharmaceutical market of Ukraine

Sales volume of domestic drugs
Sales volume of foreign drugs
Growth rate of domestic drugs
Growth rate of foreign drugs

Fig. 4. Dynamics of indicators of retail sales of antiepileptics in cash for the pharmaceutical market of Kazakhstan

Sales volume of domestic drugs
Sales volume of foreign drugs
Growth rate of domestic drugs
Growth rate of foreign drugs

Fig. 5. Dynamics of indicators of retail sales of antiepileptics in physical terms for the pharmaceutical market of Belarus

Sales volume of domestic drugs
Sales volume of foreign drugs
Growth rate of domestic drugs
Growth rate of foreign drugs
According to the results of the analysis it is established that in the market of Ukraine during 2016–2019 there is a general trend of increasing retail sales of AED, which are not included in the WHO Basic List of Essential Medicines, both in kind and in monetary terms (Fig. 7, 8). Changes in the decline in sales of this market segment could be traced only in 2020, but they are insignificant.

The results of the analysis of the number of sold packages of drugs, which are recommended by the WHO list of Essential Medicines and are part of it, during 2019–2020, show a negative trend towards decreasing the value of the indicator. At the same time, during the research period for AED included in the list of WHO Essential Medicines, annual positive indicators of growth rates of sales in monetary terms were established. However, the largest volume of sales in monetary units is provided by AED, which are not included in the WHO Basic List of Essential Medicines – 54.6 % of total sales of drugs.

The results of the study of the pharmaceutical market of Kazakhstan showed that the number of sold AED packages, which are not included in the WHO List of Essential Medicines, is increasing every year (Fig. 9). At the same time, the dynamics of the volume of these drugs in monetary terms has a wave-like character with an increase in growth rates of 3.5% in 2017 and 15.4% in 2019 (Fig. 10). During 2017–2020, there is a decrease in retail sales of AED, which are recommended by the WHO List of Essential Medicines, both in kind and in monetary terms.

The results of the analysis of retail sales of drugs in the Belarusian market in quantitative and monetary terms indicate an increase in sales of drugs for the treatment of epilepsy, which are included in the WHO Basic List of Essential Medicines and those not specified in it (Fig. 11, 12).

It was found that the growth rate for 2016–2020 AED, which is included in the WHO list of Essential Medicines, in physical terms increased by 30.1% and in monetary terms by 11.4%. Sales of drugs for the treatment of epilepsy, which are not listed by the WHO Essential Medicines, increased in 2020 compared to 2016 by 137.7% in quantitative terms and 99.0% in monetary terms. It should be noted that the largest volume of sales in monetary units is provided by drugs included in the WHO Basic List of Essential Medicines – 68.7% of total sales of AEDs in the pharmaceutical market of Belarus.
Fig. 8. Dynamics of indicators of sales volumes in cash of drugs included in the WHO Model List of Essential Medicines and other medicines for the pharmaceutical market of Ukraine

Fig. 9. Dynamics of indicators of sales volumes in physical terms of drugs included in the WHO Model List of Essential Medicines and other medicines for the pharmaceutical market of Kazakhstan

Fig. 10. Dynamics of indicators of sales volumes in cash of drugs included in the WHO Model List of Essential Medicines and other medicines for the pharmaceutical market of Kazakhstan
5. Discussion

The results of the analysis of sales of AED in the pharmaceutical markets of Ukraine in 2020 and Kazakhstan in 2017, according to which there is a tendency to reduce the indicator in physical terms, and at the same time increase its value in monetary terms. Thus, it can be argued that the negative processes that took place in different periods in the financial markets of Ukraine and Kazakhstan, led to rising prices for drugs, and had a negative impact on ensuring socio-economic affordability of pharmaceutical care for epilepsy.

The results of the pharmaceutical markets of Ukraine and Kazakhstan indicate a decrease in the number of sales of domestic AED relative to foreign. It is established that the largest volume of sales in monetary units is provided by foreign-made drugs, which in the Ukrainian market account for 80 % of total sales of AED and in the market of Kazakhstan – 95 % in 2016–2020. The established facts indicate the need to implement effective mechanisms for import substitution of AED, which, in our opinion, will provide the population of these countries with efficient, high quality and affordable AED of domestic production.

According to the results of the analysis, it is established that in the market of Ukraine during 2016-2019 there is a general trend of increasing retail sales of AED, which are not included in the WHO Basic List of Essential Medicines, both in natural and in monetary terms. In the pharmaceutical market of Kazakhstan, the number of sold AED packages that are not included in the WHO List of Essential Medicines is increasing every year. The dynamics of the indicators of the volumes
of these drugs in monetary units has a wave-like character with an increase in growth rates by 3.5% in 2017 and by 15.4% in 2019. In the market of Belarus in quantitative and monetary terms indicate an increase in sales of drugs for the treatment of epilepsy, which are included in the WHO Basic List of Essential Medicines and those not specified in it. It is established that the largest volume of sales in monetary units is provided by drugs included in the WHO Basic List of Essential Medicines – 68.7% of the total sales of AEDs in the pharmaceutical market of Belarus.

**Study limitations.** The results of the study allow us to form a more rational financial policy, which ultimately creates favourable conditions for the realization of the rights of patients with epilepsy to receive free and quality pharmaceutical and medical care. It is known to be effective conducting pharmacotherapy in the early stages of pathological development process allows in the future to significantly reduce the cost of treatment of patients with epilepsy [21, 22]. However, they can be used only when making organizational and economic decisions to improve the provision of AED.

**Prospects for further research.** In developing rational models of financing the provision of medical and pharmaceutical care for patients with epilepsy, we have identified the following areas of future research: conducting a detailed factor analysis of the impact of external and internal parameters on the dynamics of changes in AED consumption; study of the distribution of consumption according to morbidity.

6. **Conclusions**

The results of comparative analysis of AED consumption in the retail pharmaceutical markets of Ukraine, Kazakhstan, and Belarus in the period 2016-2020 show that there is a negative trend in sales of domestic AED in real terms in Ukraine and Kazakhstan. It is established that the retail pharmaceutical markets do not have drugs of the subgroup of valproic acid of domestic production. This fact should be assessed as a negative trend.

It is proved that the largest volume of sales in monetary units is provided by foreign-made drugs, which in the Ukrainian market account for 80% of total sales of AED and in Kazakhstan – 95% in 2016–2020. In our opinion, will provide an opportunity to provide the population of these countries with efficient, high-quality and affordable AED of domestic production.

It was found that in the market of Ukraine and Kazakhstan during 2016–2019 there is a general trend of increasing retail sales of AED, which are not included in the WHO Basic List of WHO, both in kind and in monetary terms. The results of the analysis of the retail sales of drugs in the Belarusian market in quantitative and monetary terms indicate an increase in sales of drugs for the treatment of epilepsy, which are included in the WHO Basic List of WHO and those not specified in it. In Belarus, the largest volume of sales in monetary terms is provided by drugs included in the WHO Basic List of WHO – 68.7%, which should be assessed as a positive trend in the development of the retail pharmaceutical market.

**Conflict of interests**

The authors declare there is no conflict of interests.

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