

## INVESTIGATING APPROACHES TO TREATING PATIENTS WITH ATRIAL FIBRILLATION BASED ON THE DEFINED DAILY DOSE

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### Abstract

Analysis of treatment protocols and updated recommendations of the European Society of Cardiology made it possible to establish current trends in improving the treatment of patients with atrial fibrillation. A retrospective study of scientific publications over the past 10 years helped determine that in 2013, 2015 was the peak of research on the treatment of atrial fibrillation.

Since the problem of atrial fibrillation disease is increasingly observed in patients of working age, we analyzed the indicators of market competition and calculated the cost of the additional dose therapy.

Calculations showed that therapy with 1 dose according to the WHO recommendations was in the study groups from 0.12 to 0.26 US dollars, which, when converted into the national currency of Ukraine, the hryvnia, indicates the availability of drugs in the studied category.

**Keywords:** *atrial fibrillation, Defined Daily Dose (DDD) concept, pharmaceutical market*

## Introduction

The prevalence of atrial fibrillation (AF), which is already a persistent cardiac arrhythmia, is increasing, even with age and the presence of structural heart disease. AF increases the risk of stroke by six times and is associated with a twofold increase in mortality, which remains above 2.5 times after correction for comorbidities, mainly caused by cerebrovascular events, progressive ventricular dysfunction and increased coronary mortality [1-3].

Patients seeking medical attention may have a newly diagnosed episode of AF or, if previous episodes have been documented, recurrent arrhythmia. The episodes themselves may be paroxysmal if they stop spontaneously, usually within seven days, or permanent if the arrhythmia persists and requires electrical or pharmacological cardioversion to stop. AF that cannot be successfully excised Cardioversion and long-term (> 1 year) AF in which cardioversion is not displayed or not done is called permanent.

There is still no consensus on whether it is better to treat patients with paroxysmal AF using strategies that target the arrhythmia itself, or those that accept the arrhythmia and control the gastric rhythm. When using frequency control strategies, arrhythmia may persist, and symptomatic improvement is achieved solely through better ventricular rate control. The most common type of AF (Fig.1).

According to a 2013 study, the estimated number of people with AF worldwide in 2010 was 33.5 million. This is about 0.5 percent of the world's population.

That is, research in the direction of therapy for patients with AF is relevant.

## Methods

The article used the generally accepted research methods: retrospective, analytical, statistical, marketing, and generalization of scientific results.

To achieve the goal of the study, we developed a phased implementation of the tasks:

Stage 1 - retrospective analysis of scientific publications on the research topic - namely, fibrillation of the forehead

Stage 2 - defining a sample of drugs for the treatment of atrial fibrillation

Stage 3 - calculating the price indicators of drug availability

Stage 4 - conclusions based on the results of the conducted research

## Results

An analysis of randomized controlled trials conducted over the past 10 years showed the availability of 2,110 publications in the National Library of America. Thus, the largest number was conducted in 2013 - 317 studies, and the smallest in 2014 - 3 studies, respectively, (Fig. 2).

Thus, most studies were multicenter controlled trials involving patients of different ages, races, and ethnicities based on living and living standards in low-, middle-, or high-income countries, and 2013, 2015, and 2016 were the most productive in terms of publications. open access research.

Thus, analyzing the information in studies, it was found that the most common are:

- Recommendations for the treatment of atrial fibrillation 2020 ESC Clinical Practice Guide

- Order of the Ministry of Health of Ukraine 15.06.2016 № 597 Unified clinical protocol of primary, secondary (specialized) and tertiary (highly specialized) medical care "Atrial fibrillation"

According to the recommendations, there are four classes of AF depending on the symptoms - moderate, severe, disability.

According to the treatment recommendations analyzed by punctures, we selected a group of drugs for calculating the price liquidity index: Co7AA05 Propranolol and Co8DB01 Diltiazem. Naturally, the list of drugs is more extensive, but we selected only those for which there is a registered retail price in the public domain and which are registered on the Ukrainian market [4-6].

So, according to the analysis for the first group, such drugs were registered:

- DIAKORDIN 60 tablets of 60 mg № 50 (10x5): 10 tablets in a blister; 5 blisters in a cardboard box, Sanofi-Aventis Ukraine. Price run: 68.70 UAH (2.57 USD) or 79.20 UAH (2.96 USD).
- DIAKORDIN® 90 RETARD coated tablets, prolonged action of 90 mg № 30 (10x3): 10 tablets in a blister; 3 blisters in a cardboard box, Sanofi-Aventis Ukraine. Price run: 87.11 UAH (3,26 USD) or 143.8 UAH (5,36 USD).

- DIAKORDIN® 120 RETARD prolonged-release tablets of 120 mg № 30 (10x3): 10 tablets in a blister; 3 blisters in a cardboard box, Sanofi-Aventis Ukraine. Price run: 97,22 UAH (3.63 USD) or 149,5 UAH (5,59 USD).

In the second group, the following drugs was presented:

- ANAPRILIN-ZDOROV`E applet 40 mg, 10 tablets in a blister; 5 blisters in a cardboard box; 50 tablets in a blister; 1 blister in a cardboard box; 50 tablets in a plastic container; 1 container Pharmaceutical company "Zdorov`e", Ukraine. Price run: 59 UAH (2.21 USD) or 67 UAH (2,51 USD)
- ANAPRILIN- ZDOROV`E tablets of 10 mg, 10 tablets in a blister; 5 blisters in a cardboard box; 50 tablets in a blister; 1 blister in a cardboard box; 50 tablets in a plastic container; 1 container in a cardboard box. Pharmaceutical company "Zdorov`e", Ukraine. Price run: 45 UAH (1.68 USD) or 148,5 UAH (5.55 USD).

This coefficient reflects the state of competition in the market and can show an analysis of the availability of drugs in a chat. The calculation of the average liquidity ratio for the group Co7AA05 Propranolol was in the range from 0.88 to 0.14. For group Co8DB01 Diltiazem 0.15, 0.64, 0.65, respectively. Thus, the calculation of the liquidity ratio showed that the problems with the breakdown by market, since the financial analysis are from 0,0 to 0.5, (Fig. 3,4), [7-9].

To carry out ATC / DDD-methodology bulky dosage DDD (defined daily dose) for the minimum amount of the drug (Table 1). The cost per dose was estimated to be between USD 0.12 and USD 0.26. The price for a course of therapy will depend on the manufacturer of the drug, as well as on the number of tablets in the package, [10-12].

### Conclusions

1. We analysed randomized trials over the past 10 years on the treatment and prevention of patients with atrial fibrillation. It was revealed that in 2013 and 2015 there was the largest number of

- published studies in the open access on the stated topic.
2. Analysis of the average maximum and minimum retail prices for the studied drug groups Co7AA05 Propranolol and Co8DB01 Diltiazem showed a price range from 1 to 6 USD. At the same time, the liquidity indicator was in the range from 0.15 to 0.88, which is typical for uneven competition in the market.
  3. The calculation DDD-methodology showed that one dose of the drug per group Co8DB01 Diltiazem cost from 0,12 to 0,15 USD and Co7AA05 Propranolol cost from 0,17 to 0,26 USD.

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## Type of AF

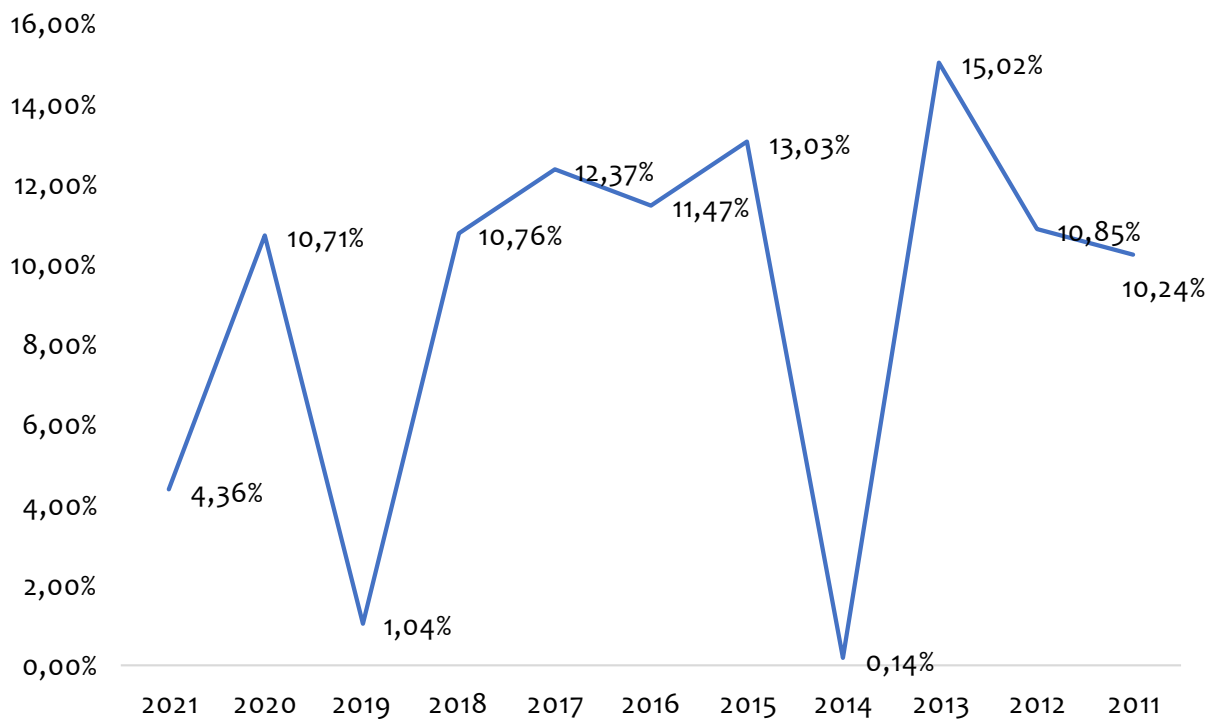
*Paroxysmal atrial fibrillation. Symptoms of atrial fibrillation come and go, usually lasting from a few minutes to an hour. Sometimes the symptoms appear within a week, and episodes may recur repeatedly. The symptoms may go away on their own. Some people with episodic A-fiber need treatment.*

*Persistent type of AF. With this type of atrial fibrillation, the heart rhythm does not return to normal by itself. If a person has symptoms of A-fibrillation, cardioversion or treatment can be used to restore and maintain a normal heart rhythm.*

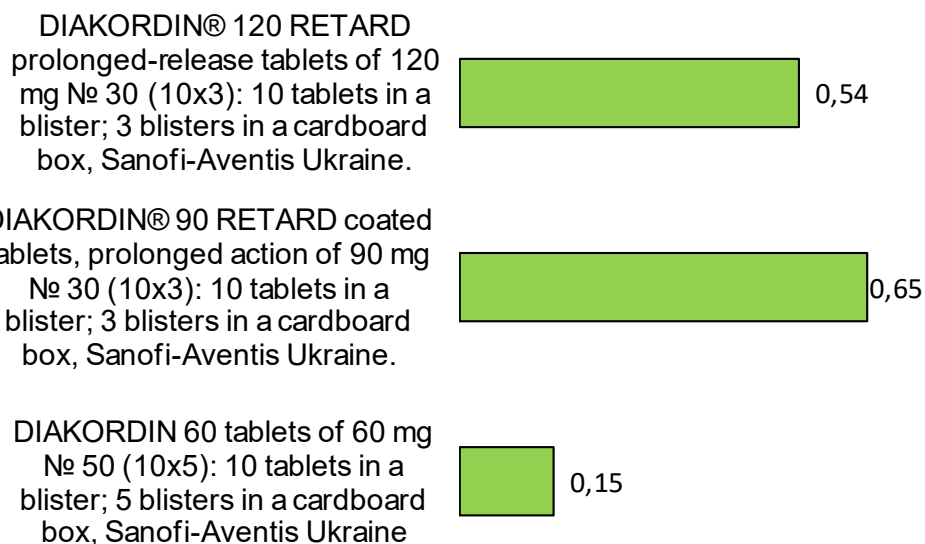
*It has been stable for a long time. This type of atrial fibrillation is continuous and lasts more than 12 months.*

*Constant. With this type of atrial fibrillation, cardiac arrhythmia is not restored. Medication is needed to control heart rate and prevent blood clots.*

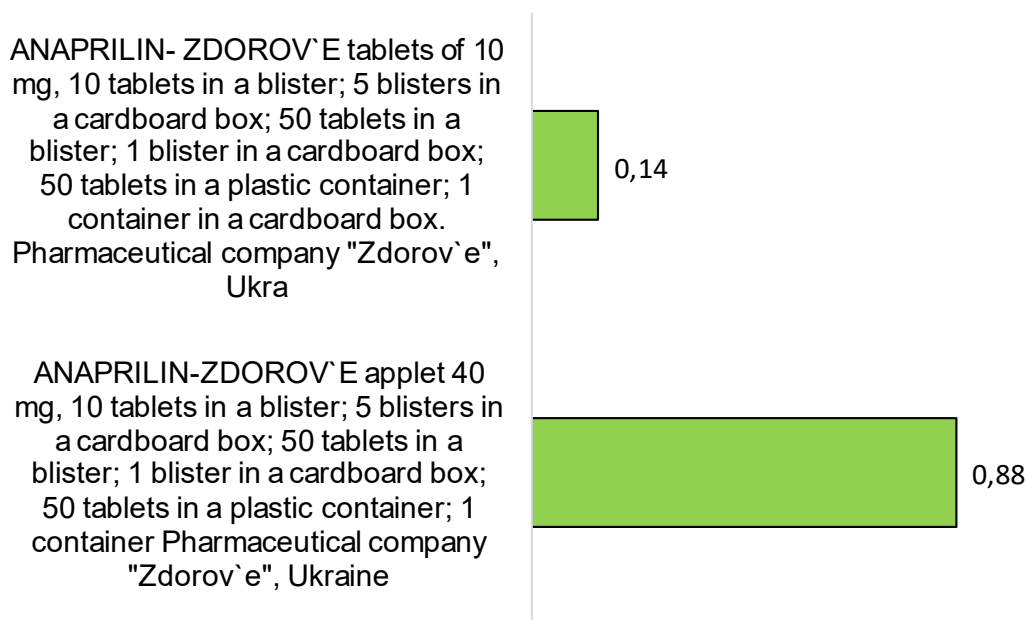
**Figure 1** The most common type of AF



**Figure 2** Proportion of randomized fibrillation studies in the last 10 years



**Figure 3** Calculation of the average liquidity indicator for the group Co8DB01 Diltiazem



**Figure 4** Calculation of the average liquidity indicator for the group Co7AA05 Propranolol

**Table 1** Calculation for drugs in the treatment of atrial fibrillation DDD

Name of the drug	ATX-code	DDD, mg	Price DDD, mg 2021	
			UAH	USD
DIAKORDIN 60 tablets of 60 mg № 50 (10x5): 10 tablets in a blister; 5 blisters in a cardboard box, Sanofi-Aventis Ukraine	C08DB01 Diltiazem	0.16	3.45	0.12
DIAKORDIN® 90 RETARD coated tablets, prolonged action of 90 mg № 30 (10x3): 10 tablets in a blister; 3 blisters in a cardboard box, Sanofi-Aventis Ukraine	C08DB01 Diltiazem	0.16	4.35	0.16
DIAKORDIN® 120 RETARD prolonged-release tablets of 120 mg № 30 (10x3): 10 tablets in a blister; 3 blisters in a cardboard box, Sanofi-Aventis Ukraine	C08DB01 Diltiazem	0.16	3.24	0.12
ANAPRILIN-ZDOROV`E applet 40 mg, 10 tablets in a blister; 5 blisters in a cardboard box; 50 tablets in a blister; 1 blister in a cardboard box; 50 tablets in a plastic container; 1 container Pharmaceutical company "Zdorov`e", Ukraine	C07AA05 Propranolol	0.24	7.08	0.26
ANAPRILIN- ZDOROV`E tablets of 10 mg, 10 tablets in a blister; 5 blisters in a cardboard box; 50 tablets in a blister; 1 blister in a cardboard box; 50 tablets in a plastic container; 1 container in a cardboard box. Pharmaceutical company "Zdorov`e", Ukraine	C07AA05 Propranolol	0.24	4.35	0.17