

# Cost analysis of migraine pharmacotherapy with selective 5HT<sub>1</sub> receptor agonists in Ukraine

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## Abstract

The cost analysis for the relief of migraine attack using selective 5HT<sub>1</sub>-receptor agonists (frovatriptan, zolmitriptan, rizatriptan, sumatriptan) of domestic and imported manufacturers in various dosages and forms of production in the proposed resource online pharmacy chains of Lviv for their efficient and cost effective applications. Among the registered drugs, most dosage forms and trade names are presented for sumatriptan; slightly less for rizatriptan and zolmitriptan; for frovatriptan is only one trade name. It has been found that to relieve migraine attack with domestic drugs will be cheaper for patients than imported. Packaging with the same dosage of active ingredient, but with more tablets in the blister is more cost effective for patients. It's the most economical to stop the migraine attack with Stopmigran (sumatriptan) at a dosage of 50 mg, packing 6 tablets in a blister, and the most valuable drug is Rapimig (zolmitriptan) at a dosage of 50 mg, packing 6 tablets in a blister.

## Keywords

selective 5HT<sub>1</sub>-receptor agonists, zolmitriptan, rizatriptan, sumatriptan, frovatriptan, cost of pharmacotherapy, migraine attack

## Introduction

Today, migraine is one of the most widespread and socially significant diseases, as around 12% of the population in the world suffer from it. In 2000, migraine was included in the list of diseases of global importance and is a social burden for humanity (Murray and Lopez 1996). According to data of Migraine research foundation migraine is the third most prevalent and the sixth most disabling illness in the world (<https://migraineresearchfoundation.org/about-migraine/migraine-facts/>).

According to the summary edited by Murray and Lopez (1996) migraines are most commonly detected for people of age 35–40 years, with men accounting for 2–15% and women accounting for 6–25% of the population. Although women experience migraine pain attacks

2–3 times more often than men, the intensity of pain is usually higher in men (Oros et al. 2017).

In terms of diagnosis and treatment costs, migraine ranks 20<sup>th</sup> among all existing diseases. They are related to the opening of a sick leaf: from the issuance of a certificate of incapacity to payment, the decline in the efficiency of patients, and the cost of inadequate diagnostic procedures and appropriate therapy. Thus, migraine is now considered as a chronic brain disease, which leads to severe maladaptation of patients and significant economic losses (Oros et al. 2017).

According to the Ministry of Health of Ukraine for relief of migraine attack are used non-specific treatment – analgesics, nonsteroidal anti-inflammatory drugs, combination therapies and specific treatment – selective 5ht<sub>1</sub>-receptor agonists, ergotamine drugs (Order No. 487 dated

17.08.2007. approval of clinical protocols of rendering medical care in specialty “Neurology”). Both ergotamine and selective serotonin 5-HT(1B/1D) receptor agonists (‘triptans’) are currently used in the treatment of moderate to severe migraine. Ergotamine is a traditional therapy with a lower drug acquisition cost compared with triptans (Zhang and Hay 2005), but not registered in Ukraine.

It was showed that triptans are more efficacious than ergotamine, but the higher acquisition costs and shorter duration of action are disadvantages of triptans compared with ergotamine (Zhang and Hay 2005).

**The aim of the research** was to compare the costs of the initial treatment of migraine attack using selective 5HT1-receptor agonists from domestic and imported manufacturers in different dosages and release forms in the resource-offered pharmacy networks in Lviv for their rational use for patients.

## Materials and methods of the research

Objects: medicines registered in Ukraine – selective 5HT1 receptor agonists – sumatriptan, rizatriptan, zolmitriptan, frovatriptan; price information from the online drug search service “GeoApteka” (December 2019) for the searches that match the trade names of the above-mentioned drugs.

Methods: webometric and benchmarking, pharmacoeconomic analysis (cost minimization).

To find the value of drugs, we lead the trade name of sumatriptan (obtained from the website State Drug Register of Ukraine (SDRU), indicating the dosage of the active substance and the number of tablets in the pack. The calculation of the cost of 1 tablet of sumatriptan, regardless of the trade name of the drug was performed by the formula:

$$1 \text{ tablet} = \frac{\text{cost of 1 pack of sumatriptan (50 or 100 mg)}}{\text{quantity of tablets (capsules) per pack}}$$

The average cost of 1 tablet was calculated by the formula:

$$Ca = \frac{x1}{x2}$$

where X1 – the sum of the prices of 1 tablet for a specific trade name of the drug in all the offered pharmacies in the service “GeoApteka”.

X2 – the number of pharmacies that have a specific drug, which is reflected in the service “GeoApteka”.

We calculated the cost of 1 seizure therapy with the maximum possible dose of sumatriptan according to the formula:

$$DDD_{50} = Ca_{50} * 6,$$

where  $DDD_{50}$  – day drug dosage sumatriptan taken with 50 mg tablets.

$Ca_{50}$  – average cost of 1 tablet of 50 mg.

6 – number of tablets of 50 mg sumatriptan to be taken for maximum dose (300 mg).

$$DDD_{100} = Ca_{100} * 3,$$

where  $DDD_{100}$  – day drug dosage sumatriptan taken with 100 mg tablets.

$Ca_{100}$  – average cost of 1 tablet of 100 mg.

3 – number of tablets of 100 mg sumatriptan to be taken for maximum dose (300 mg).

The calculation of the cost of 10 mg of rizatriptan, regardless of the trade name of the drug 10 mg was performed by the formula:

$$1 \text{ dose (10 mg)} = \frac{\text{cost of 1 pack of rizatriptan (10 mg)}}{\text{number of tablets (capsules) per pack}}$$

The average cost of 1 tablet was calculated by the formula given for sumatriptan.

The calculation of the cost of therapy 1 attack the maximum possible dosage of rizatriptan was performed by the formula:

$$DDD_{10 \text{ mg}} = Ca * 2,$$

where  $DDD_{10 \text{ mg}}$  – daily dose of rizatriptan taken with 5 mg tablets.

$Ca$  – the average cost of 1 dose of rizatriptan is 10 mg.

2 – number of doses of 10 mg of rizatriptan to be taken for maximum dose (20 mg).

The calculation of the cost of 1 dose of zolmitriptan, regardless of the trade name of the drug 2.5 mg was performed by the formula:

$$1 \text{ dose (2.5 mg)} = \frac{\text{cost of 1 pack of zolmitriptan (2.5 mg)}}{\text{number of tablets per pack}}$$

The calculation of the cost of 5 mg of zolmitriptan, regardless of the trade name of the drug 5 mg was performed by the formula:

$$1 \text{ dose (5 mg)} = \frac{\text{cost of 1 packet of zolmitriptan (5 mg)}}{\text{number of tablets per pack}}$$

The average cost of 1 tablet was calculated by the formula given for sumatriptan.

The calculation of the cost of therapy 1 attack the maximum possible dosage of zolmitriptan was performed by the formula:

$$DDD_{2.5 \text{ mg}} = Ca * 4,$$

where  $DDD_{2.5 \text{ mg}}$  – daily dose of zolmitriptan taken in 2.5 mg dosage form.

$Ca$  – the average cost of 1 dose of zolmitriptan 2.5 mg.

4 – number of doses of 2.5 mg of zolmitriptan to be taken to achieve the maximum daily dose (10 mg) or:

$$DDD_{5 \text{ mg}} = Ca * 2,$$

where  $DD_{5 \text{ mg}}$  – daily dose of zolmitriptan taken in 5 mg dosage form.

$Ca$  – the average cost of 1 dose of zolmitriptan 5 mg.

2 – number of doses of 5 mg of zolmitriptan to be taken to achieve the maximum daily dose (10 mg).

## Results

According to the State Drug Register of Ukraine (SDRU) (<http://www.drlz.com.ua>), in December 2019 were registered 4 international non-proprietary names of selective 5HT<sub>1</sub> receptor agonists: sumatriptan (N02CC01) – 15 trade names (TN) taking into account the dose of the active substance and the amount of dosage form in the immediate packaging; rizatriptan (N02CC04) – 6 TN; zolmitriptan (N02CC03) – 7 TN; frovatriptan (N02CC07) – 1 TN.

Mild or moderate migraines are often treated with aspirin, acetaminophen, nonsteroidal anti-inflammatory drugs, antiemetic drugs, or isometheptene. Triptans are used to treat moderate or severe migraine and when nonspecific medications have been ineffective. Sumatriptan, the first triptan used, is effective but can induce adverse events, second-generation triptans (zolmitriptan, naratriptan, rizatriptan, and almotriptan) were developed to increase the benefit-to-risk ratio in the migraine management. Important pharmacologic, pharmacokinetic, and clinical differences exist among those drugs, but the tolerability profile of the newest triptans is very good, and they provide rapid relief from headache and sustained the duration of effect (Gallagher and Cutrer 2002). For patients with more severe migraines, implementing a stratified approach to treatment using migraine-specific medication at the beginning of the acute treatment is cost-effective for most patients. Stratified care not only improves results and reduces performance, but also reduces costs (Adelman and Belsey 2003).

“GeoApteka” (<https://geoapteka.ua/>) internet service provides an opportunity to receive up-to-date information on the availability, cost and sales points of the required drugs. To calculate the average price, maximum permissible daily dose we used formulas which are in the section “Materials and methods of the research”.

According to the instructions for the medical use of Sumatriptan (available on line from <http://www.drlz.com.ua>), it is recommended to use it as early as possible after the onset of migraine, although it is equally effective at every stage. The recommended dose of sumatriptan for adults is 50 mg. In some cases, the dose may be increased to 100 mg. Tablets with the appropriate active ingredient content should be used to achieve the appropriate dosage. The total daily dose within 24 hours should not exceed 300 mg.

Table 1 shows the cost of 1 tablet and the average price of 300 mg sumatriptan as the maximum permissible daily dose.

In view of the fact that the treatment of migraine attack with sumatriptan is recommended to start with a 50 mg dose, we first compared the prices of drugs with the corresponding dosage.

According to information from the “GeoApteka” search service, domestic drugs selective agonists of 5HT<sub>1</sub> seroto-

**Table 1.** Sumatriptan-based drugs assortment registered in Ukraine with price indicators (UAH) for the initial relief of migraine attacks and maximum daily dose of drugs.

№	Trade name	Manufacturer country	Average price for 1 dose/ max dose (UAH)			
			Tablets	Tablets coated	Tablets coated with a film sheath	Capsules
1	Amigraine 50 mg №1	Ukraine	”_“	”_“	”_“	21,63/129,78
2	Amigraine 50 mg №3	Ukraine	”_“	”_“	”_“	19,55/117,30
3	Amigraine 100 mg №1	Ukraine	”_“	”_“	”_“	44,07/132,21
4	Amigraine 100 mg №3	Ukraine	”_“	”_“	”_“	29,93/89,78
5	Antymi-graine-Zdorovya 50 mg №1	Ukraine	”_“	”_“	22,41/ 134,46	”_“
6	Antymi-graine-Zdorovya 50 mg №3	Ukraine	”_“	”_“	24,02/ 144,10	”_“
7	Antymi-graine-Zdorovya 100 mg №1	Ukraine	”_“	”_“	45,24/ 135,72	”_“
8	Antymi-graine-Zdorovya 100 mg №3	Ukraine	”_“	”_“	45,28/ 135,83	”_“
9	Imigran 50 mg	Poland	”_“	+	”_“	”_“
10	Megrefit 50 mg	Germany	+		”_“	”_“
11	Megrefit 100 mg	Germany	+		”_“	”_“
12	Migranol 50 mg №10	Canada		32,39/194,37	”_“	”_“
13	Stopmigraine 50 mg №6	Ukraine	”_“	”_“	17,96/ 107,76	”_“
14	Stopmigraine 100 mg №3	Ukraine	”_“	”_“	33,02/ 99,07	”_“
15	Sumamigraine 50 mg №2	Poland	”_“	44,24/265,46	”_“	”_“
16	Sumamigraine 100 mg №2	Poland	”_“	87,01/261,03	”_“	”_“
17	Sumafix 50 mg	India	+	”_“	”_“	”_“
18	Sumafix 100 mg	India	+	”_“	”_“	”_“

”\_“ – not registered in Ukraine.

+ – registered in Ukraine, but not available in the pharmaceutical market.

nin receptors are available in most pharmacies / pharmacy chains in the city of Lviv (information from 14 pharmacy chains is provided on the site). The price for domestic preparations of sumatriptan 50 mg (1 tablet) ranges from 14.41 to 26.73 UAH. The average price is 20.44 UAH. The average cost of 1 tablet of sumatriptan 50 mg under the trade name Antymigraine-Zdorovya in packs of 1 tablet in a blister costs 1.07 times cheaper than in packs of 3 tablets in a blister. Amigraine in 1 capsule pack is 1.10 times more expensive than 3 capsules in a blister pack. Stopmigraine drug information is only for tablets of 6 in a blister.

From the 5 registered trade names of Sumatriptan imported (regardless of the country of origin of the drugs) in the dosage of 50 mg of active substance, the site “GeoApteka” contains information only about prices of 2 drugs Sumamigraine and Migranol. The price of drugs ranges from 30.14 (Migranol) to 49.50 UAH (Sumamigran). The average price of 1 tablet of imported sumatriptan is 38.29 UAH.

It was established that the most of Sumatriptan-based medicines in the pharmaceutical market are manufactured in Ukraine (10); in Poland - 3 drugs; 2 drugs each in Germany and India; in Canada – 1 drugs.

It was established that the pharmaceutical market of Ukraine has an original drug of Sumatriptan – Sumami-

**Table 2.** Range and average cost of 1 tablet of sumatriptan in pharmaceutical market of Ukraine.

Trade name of drugs	Price ranges from....to....	Average cost
Amigraine 50 mg	15.66 to 20.33 UAH	19.55 UAH (for packs of 3 capsules per blister)
Amigraine 50 mg	18.20 to 23.85 UAH	21.63 UAH (for packs of 1 capsule per blister)
Amigraine 100 mg	35.75 to 47.40 UAH	44.07 UAH (for packs of 1 capsule per blister)
Amigraine 100 mg	25.65 to 32.66 UAH	29.93 UAH. (for packs of 3 capsules per blister)
Antymigraine-Zdorovya 50 mg	18.40 to 26.00 UAH	22.41 UAH (for packs of 1 tablet in a blister)
Antymigraine-Zdorovya 50 mg	19.83 to 26.73 UAH	24.02 UAH (for packs of 3 tablets in a blister)
Antymigraine-Zdorovya 100 mg	38.42 to 49.70 UAH	45.24 UAH (for packs of 1 tablet in a blister)
Antymigraine-Zdorovya 100 mg	38.47 to 47.73 UAH	45.28 UAH (for packs of 3 tablets in a blister)
Imigran	information on the search service unavailable	
Megrefit	information on the search service unavailable	
Migranol	30.14 to 34.65 UAH	32.39 UAH (for packs of 10 tablets in a blister)
Stopmigraine 50 mg	14.41 to 20.99 UAH	17.96 UAH (for packs of 6 tablets in a blister)
Stopmigraine 100 mg	27.50 to 37.61 UAH	33.02 UAH. (for packs of 3 tablets in a blister)
Sumamigraine 50 mg	41.48 to 49.50 UAH	44.24 UAH (for packs of 2 tablets in a blister)
Sumamigraine 100 mg	75.97 to 95.62 UAH	87.01 UAH (for packs of 2 tablets per blister)
Sumafiks	information on the search service unavailable	

gren, which maximum daily dose is 300 mg. Cost of pharmacotherapy taken with 50 mg tablets is 2.26 times more expensive and taken with 100 mg tablets is 2.90 times more expensive than the cheapest domestic generic drug – Amigraine (Table 2).

It is found that the average cost of 1 tablet of sumatriptan 50 mg of domestic production is 1.87 times cheaper than the imported one.

In migraine attacks of moderate or moderate severity, as well as in the recommendation of a doctor, it is possible to start cupping of a seizure with sumatriptan at a dosage of 100 mg. The cost of 100 mg Sumatriptan 100 mg (1 tablet) ranges from 25.65 (Amigraine) to 49.70 (Antymigraine-Zdorovya) in UAH. The average price is 38.04 UAH. The average cost of 1 tablet of sumatriptan 100 mg under the trade name Antymigraine-Zdorovya in packs of 1 tablet in a blister costs 1.47 times more expensive than in packs of 3 tablets in a blister. Amigraine in 1 capsule pack costs almost the same as 3 capsules in a blister. Stopmigraine drug information is only for tablets of 3 pieces in a blister.

From the 5 registered trade names of Sumatriptan imported (regardless of the country of origin of the drugs) in the dosage of 100 mg of active ingredient, the “GeoApteka” website only has information about the prices of 1 drug – Sumamigraine. The price of drugs ranges from 75.97 to 95.62 UAH. The average price of 1 tablet of imported sumatriptan 100 mg is 87.01 UAH. It is found that the average cost of 1 tablet of sumatriptan 100 mg of domestic production is 2.28 times cheaper than the imported one.

According to the data obtained from the SDRU, it is established that at present, only 1 trade name of capsule sumatriptan is registered in Ukraine – Amigraine (domestic production); pills – Megrefit and Sumafix; coated tablets – Imigran, Migranol, Sumamigraine; film-coated tablets – Antymigraine-Zdorovya, Stopmigraine. No injectable sumatriptan dosage form has been reported.

The next stage of the study was the processing of information about Rizatriptan drugs registered in Ukraine. In studying the instructions to rizatriptan was found that the recommended dose relieve migraine attacks adults is 10 mg. The maximum daily dose is 20 mg (available on line from <http://www.drlz.com.ua>).

As dosage forms of rizatriptan in doses of 5 and 10 mg were registered in Ukraine, we calculated the initial dose for all drugs - 10 mg. However, at the “GeoApteka” service there is no information about the prices of drugs in the dosage of 5 mg, therefore no calculations were made. To calculate the average price, maximum permissible daily dose we used formulas which are in the section “Materials and methods of the research”.

The original drug of Rizatriptan is not registered in Ukraine.

We calculated the average price of 20 mg of rizatriptan as the maximum permissible daily dose (Table 3).

**Table 3.** Assortment of rizatriptan-based drugs registered in Ukraine with cost indicators (UAH) for the initial relief of migraine attacks and maximum daily dose of drugs.

Trade name	Manufacturer country of drug	Average price for 1 dose/ max dose (UAH)	
		Tablets	Pills that are dispersed in the oral cavity
Rizamigraine 5 mg №1	Ukraine	+	”-“
Rizamigraine 5 mg №3	Ukraine	+	”-“
Rizatriptan-Farmaten 5 mg № 2	Greece	”-“	+
Rizatriptan-Farmaten 10 mg № 2	Greece	”-“	+
Rizoptan 10 mg № 3	Ukraine	40,80/81,61	”-“
Rizoptan 10 mg № 6	Ukraine	36,50/73,01	”-“
Rizoptan 10 mg № 9	Ukraine	33,19/66,39	”-“

”-“ – not registered in Ukraine.

+ – registered in Ukraine, but not available in the pharmaceutical market.

It has been established that in Ukraine, rizatriptan is presented in the form of tablets and tablets dispersed in the oral cavity; production of Ukraine and Greece.

In the course of the research it was found that there are no prices for imported rizatriptan – Rizatriptan-Farmaten for 5 and 10 mg of the production of Greece in the form of tablets dispersed in the oral cavity and for domestic tablets – Rizamigraine. Only information about 1 domestic medicinal product – Rizoptan is presented.

So, according to the service “GeoApteka” cost of 1 tablet of rizatriptan-based drugs is shown (Table 4).

It is found that is economically more convenient for patients to buy the specified drug at 10 mg in package of 9,

**Table 4.** Range and average cost of 1 tablet of rizatriptan in pharmaceutical market of Ukraine.

Trade name of drugs	Price ranges from....to....	Average cost
Rizamigraine 5 mg №1		information on the search service unavailable;
Rizamigraine 5 mg №3		information on the search service unavailable;
Rizatriptan – Farmaten 5 mg №2		information on the search service unavailable;
Rizatriptan – Farmaten 10 mg №2		information on the search service unavailable;
Rizoptan 10 mg	30.33 to 44.16 UAH	40.80 UAH (for packs of 3 tablets in a blister);
Rizoptan 10 mg	32.41 to 38.70 UAH	36.50 UAH (for packs of 6 tablets in a blister)
Rizoptan 10 mg	26.98 to 35.44 UAH	33.19 UAH (for packs of 9 tablets in a blister)

then stopping a migraine attack will cost 1.23 times cheaper than the same dosage, but with a package of 3 tablets.

Further research we conducted for drugs zolmitriptan. It is established that currently in Ukraine there are 3 dosage forms of 2.5 and 5 mg of zolmitriptan – nasal spray, film-coated tablets and mouth-dispersed. Each dosage form is manufactured by only 1 manufacturer. According to the instructions for tableted forms of zolmitriptan and nasal spray relief of migraine attack should begin with a dosage of 2.5 mg. If the dose is not effective at 2.5 mg, it is possible to increase the single dose to 5 mg (higher single dose). The highest daily dose should not exceed 10 mg (available on line from <http://www.drlz.com.ua/>).

As zolmitriptan dosage forms of 2.5 and 5 mg were registered in Ukraine, we calculated the initial dose of drugs – 2.5 mg.

To calculate the average price, maximum permissible daily dose we used formulas which are in the section “Materials and methods of the research”.

The original drug of Zolmitriptan is not registered in Ukraine.

It was calculated average price of 10 mg of zolmitriptan as the maximum permissible daily dose (Table 5).

**Table 5.** Assortment of drug-based zolmitriptan, which are registered in Ukraine with value indicators (UAH) for the initial relief of migraine attacks and maximum daily dose of drugs.

Trade name	Manufacturer country of drugs	Average price for 1 dose/ max dose (UAH)		
		Nasal spray	Film coated tablets	Tablets, dispersible oral
Zolmigraine spray 2.5 mg/2 ml – 20 doses	Ukraine	+	”-“	”-“
Zolmigraine spray 5 mg/2 ml – 20 doses	Ukraine	+	”-“	”-“
Zolmigraine 2.5 mg №2	Ukraine	”-“	35,38/141,55	”-“
Zolmigraine 2.5 mg №10	Ukraine	”-“	22,73/90,94	”-“
Rapimig 2.5 mg №2	Malta	”-“	”-“	50,88/203,52
Rapimig 2.5 mg №6	Malta	”-“	”-“	39,81/159,24
Rapimig 5 mg №2	Malta	”-“	”-“	85,92/171,84
Rapimig 5 mg №6	Malta	”-“	”-“	57,84/115,68

”-“ – not registered in Ukraine.

+ – registered in Ukraine, but not available in the pharmaceutical market.

**Table 6.** Cost of 1 tablet of zolmitriptan in pharmaceutical market of Ukraine.

Trade name of drugs	Price ranges from....to....	Average cost
Zolmigraine 2.5 mg spray in vials		no information on search service
Zolmigraine 5 mg spray in vials		no information on search service
Zolmigraine 2.5 mg	29.25 to 38.00 UAH	35.38 UAH (for packs of 2 tablets in a blister)
Zolmigraine 2.5 mg	20.14 to 23.65 UAH	22.73 UAH. (for packs of 10 tablets in a blister)
Rapimig 2.5 mg	34.32 to 42.00 UAH	39.81 UAH (for packs of 6 tablets in blister packs)
Rapimig 2.5 mg	49.01 to 52.75 UAH	50.88 UAH (for packs of 2 tablets in a blister)
Rapimig 5 mg	80.25 to 92.25 UAH	85.92. (for packs of 2 tablets in a blister)
Rapimig 5 mg	46.33 to 66.99 UAH	57.84 UAH. (for packs of 6 tablets in blister packs)

It was established that in Ukraine, zolmitriptan is presented in film coated tablets and oral dispersible tablets and nasal spray; production of Ukraine and Malta.

In the course of the research it was found that on the used search internet service there are no prices for domestic nasal spray of zolmitriptan – Zolmigraine 2.5 and 5 mg. The average cost of 1 tablet of zolmitriptan 2.5 mg under the trade name of Zolmigraine (domestic production) is 29, 05 UAH; drug in packs of 2 tablets in a blister costs in 1.55 times more expensive than in packs of 10 tablets in a blister.

Rapimig (imported drugs) in a pack of 2 tablets in a blister costs 1.27 times more expensive than in packs of 6 tablets in a blister, and the average cost is 45.34 UAH. The average cost of 1 tablet of zolmitriptan 5 mg under the trade name Rapimig (imported drugs) ranges from 46.33 to 92.25, the average cost is 71.88 UAH. Packing 2 tablets in a blister costs 1.48 times more expensive than packing 6 tablets in a blister. Therefore, packing with the same dosage of the active substance but with more tablets in the blister is more economical for patients.

So, according to the data of service “GeoApteka” cost of 1 tablet of zolmitriptan-based drugs is shown (Table 6).

It is found that the average cost of 1 tablet of zolmitriptan 2.5 mg of domestic production is 1.56 times lower than the imported one.

The final stage of the study was the drug frovatriptan – the latest in the pharmaceutical market of Ukraine.

According to the SDRU, currently in Ukraine only 1 drug – film coated tablets of 2.5 mg, 2 or 6 tablets in blisters – Frovamigran, made in Italy, has been registered. According to the instructions for this drug, the initial dose for the relief of migraine attack is 2.5 mg. The total daily dose of frovatriptan should not exceed 5 mg (available on line from <http://www.drlz.com.ua/>). We have not made any calculations for this drug because the information on the “GeoApteka” search service is unfortunately unavailable.

## Discussion

To determine the cost-effectiveness of the triptans, a meta-analysis was conducted of the efficacy data from 27 oral triptan trials, using the endpoint of “pain-free” status within 2 hours after initial dosing as the indicator of efficacy. Efficacy data were used to determine the number needed to treat to achieve pain-free status in 1 patient within 2 hours postdose and then applied the per-dose costs for each triptan to the number needed to treat values. From a population health perspective, the lower acquisition cost of almotriptan 12.5 mg allows for effective treatment of more patients than rizatriptan 10 mg for no additional medication cost (Derry et al. 2014).

It was investigated the efficacy and tolerability of sumatriptan in the treatment of acute migraine attacks in adults by four routes of administration (oral, subcutaneous, intranasal, and rectal) compared with both placebo and active comparators. The most effective dose of sumatriptan for each route of administration for the outcome of headache relief (pain reduced from moderate or severe to none or mild) at two hours was oral 100 mg, subcutaneous 6 mg, intranasal 20 mg, and rectal 25 mg. Sumatriptan is an effective abortive treatment for acute migraine attacks, but is associated with increased adverse events relative to placebo. The route of administration influences efficacy, particularly within the first hour after administration. Subcutaneous sumatriptan shows the greatest efficacy in terms of pain relief, but at the expense of relatively high levels of adverse events, and with a high financial cost compared with other routes. Information about the relative efficacy of the different routes of administration for different outcomes should help to inform decisions about the suitability of sumatriptan as a migraine treatment, as well as about the most appropriate way to administer the treatment for individual patients (Adelman et al. 2004)

The cost-effectiveness of rizatriptan was compared with sumatriptan. The study of Zhang L and Hay J.W further showed that rizatriptan is more cost effective than sumatriptan, as evidenced by its lower cost and greater effectiveness (Zhang and Hay 2005). The efficacy of zolmitriptan for stopping an acute migraine attack was shown in a study where the authors demonstrated that zolmitriptan at a dosage of 2.5 mg had the same efficacy for acute migraine attacks as eletriptan 2.5 mg and sumatriptan 50 mg. Zolmitriptan was also more effective than naratriptan 2.5 mg (Shagbazyan et al. 2017).

The aim of study was to assess the relative cost-effectiveness of almotriptan and rizatriptan in the treatment of acute migraine. A model was built to compare almotriptan 12.5 mg and rizatriptan 10 mg for the treatment of a single, acute migraine attack. Mean and incremental cost-effectiveness ratios were calculated. The effectiveness measure was the proportion of patients who achieved sustained freedom from pain with no adverse events. Data on sustained pain-free outcomes and adverse-event rates were obtained from a meta-analysis of oral triptan trials. Efficacy and tolerability were assumed to be independent in the base-case scenario, so the total direct cost

of treating a single migraine attack was calculated, adding drug costs to health service costs per attack. Almotriptan 12.5 mg was more cost-effective than rizatriptan 10 mg for the treatment of acute migraine in this analysis based on published data (Paul Williams and Reeder 2003).

In one of the studies using a standard WHO approach to cost-effectiveness analysis (CHOICE), were modelled core set intervention strategies for migraine, taking account of coverage and efficacy as well as non-adherence. The setting was primary health care including pharmacies. Twenty six intervention strategies implemented during 10 years were modelled. These included first-line acute and prophylactic drugs, and the expected consequences of adding consumer-education and provider-training. Total population-level costs and effectiveness (healthy life years gained) were combined to form average and incremental cost-effectiveness ratios. Runs of the model for the general populations of China, India, Russia and Zambia were executed (Linde et al. 2015).

Self-management with simple analgesics was by far the most cost-effective strategy for migraine treatment in low- and middle-income countries and represents a highly efficient use of health resources. Consumer education and provider training are expected to accelerate progress towards desired levels of coverage and adherence, cost relatively little to implement, and can therefore be considered also economically attractive. Evidence-based interventions for migraine should have as much a claim on scarce health resources as those for other chronic, non-communicable conditions that impose a significant burden on societies (Linde et al. 2015).

In the course of our study, was conducted a comparative analysis of the cost of triptans-based dosage forms registered in Ukraine and their economic accessibility for patients was examined.

We found that:

- the average cost of 1 tablet of sumatriptan 50 mg of domestic production is 1.87 times lower than the imported one.
- the average cost of 1 tablet of zolmitriptan 2.5 mg of domestic production is 1.56 times lower than the imported one.

It is found that:

- The original drug Sumamigren (maximum daily dose – 300 mg), taken with 50 mg tablets is in 2.26 times more expensive and taken with 100 mg tablets is in 2.90 times more expensive than the cheapest domestic generic drug – Amigraine.
- Amigrene in 1 capsule pack costs is in 1.10 times more expensive than 3 capsules in a blister pack.
- Risoptan at 10 mg in package of 3 tablets will cost 1.23 times more expensive than the same dosage, but with a package of 9 tablets in a blister.
- Rapimig in packing 2 tablets in a blister costs 1.48 times more expensive than packing 6 tablets in a blister.

## Limitation

We study only triptans (specific drugs to treat migraine) registered on the pharmaceutical market of Ukraine with price indicators to Lviv (one of the major cities).

## Conclusions

From the end of 2019, it has been established that among the registered drugs selective 5HT<sub>1</sub>-receptor agonists most dosage forms and trade names are for sumatriptan,

slightly less for rizatriptan and zolmitriptan; for frovatriptan there is only one trade name.

It is found that the relief of migraine attack by domestic drugs will cost less to patients than imported. Packaging with the same dosage of the active ingredient, but with more tablets in the blister is more cost effective for patients.

The most cost effective for patients to stop the migraine attack is Stopmigran (sumatriptan) at a dosage of 50 mg, packing 6 tablets in a blister.

The most valuable drug for stopping migraine attack in the initial (minimum) dose is Rapimig (zolmitriptan) at a dosage of 2.5 mg, packing 6 tablets in a blister.

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