

Comparative analysis of availability and affordability of hypoglycaemic medicines for Ukrainian patients during the war 2022-2023

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Abstract

Purpose: Diabetes care, particularly type 2 diabetes (T2D), is recognised as a growing challenge in emergency situations. During the humanitarian crisis of war in Ukraine, it is important to focus on ensuring that patients have access to essential medicines for T2D. Since 1 April 2017, the Ministry of Health of Ukraine has been implementing the government programme "Affordable medicines". The List of reimbursed medicines necessary for the treatment of hypertension, diabetes and bronchial asthma includes 3 glucose lowering medicines (GLMs) - gliclazide, metformin, glibenclamide. From 01 April 2019, electronic prescribing has been implemented as part of the "Affordable Medicines" programme. It is important to investigate changes in the availability and affordability of GLMs for the treatment of T2D during the war and future directions in 2022-2023 in Ukraine.

Methods: Information from the State Register of Medicinal Products of the Ministry of Health of Ukraine from March 2023 and February 2022 (before the start of the war) was the subject of the study. Marketing, analytical, graphical, generalisation analyses were applied. Analysis of the cost of 1 DDD GLM according to the WHO ATC/DDD index and solvency ratio analysis were applied.

Results: This study is based on actual data from before the war in Ukraine and now shows that the affordability and availability of GLMs during the war in 2022-2023 has not changed dramatically. The 'Affordable Medicines' program was stably implemented, with €111.9 million allocated in 2023 and within 6 months of 2023. The National Health Service of Ukraine reimbursed €42.8 million to pharmacies for the Reimbursement List. Most Ukrainian manufacturers and foreign GLMs are very affordable due to the reimbursement system. From October 2023, 23 names of test stripes were included in the Reimbursement list of the "Affordable medicines" programme. However, foreign GLMs of innovative groups are moderately affordable for the working population based on the calculated solvency ratio.

Conclusions: Our study revealed that despite the challenges of war, the healthcare system in Ukraine remains robust, particularly in ensuring stable access to pharmaceuticals for diabetes treatment. The "Affordable Medicines" programme and the Reimbursement List are updated twice a year, and the introduction of the new drugs for T2D and diabetes insipidus was completed in 2022. Thus, the innovative GLMs, despite being registered on the market in 2022, such as Semaglutide, Semaglutide and Dapagliflozin, are not affordable in 2023. A prospective trend is the inclusion of innovative GLMs for diabetes better care on the reimbursement list.

Humanitarian crises are a major public health challenge in many countries. They can disrupt health services and limit national access to human, financial and technical resources.^[1,2] The timing of the war in Ukraine since 24 February 2022 has had a major negative impact on the supply of medicines to patients due to the breakdown of logistical supply chains, some warehouses and manufacturers could be destroyed, leading to drug shortages and subsequent increases in drug prices.^[3-5] In some areas of the eastern and southern regions of Ukraine (major war zones), access to medicines and equipment for chronically ill patients is extremely limited due to insecure delivery.^[6]

Health care systems are often damaged, inadequate and ill-equipped to meet chronic care needs.^[7] Diabetes care is recognised as a growing challenge in emergency situations, particularly in low- and middle-income countries.^[8] Often the burden of diabetes is not considered and the problems of patients with diabetes (PWD) are not adequately addressed.^[8] Therefore, during wartime, it is important to focus on ensuring that patients have access to the medicines necessary, for example, to treat type 2 diabetes (T2D).^[9-11]

Since 2017, the first reimbursement programme "Affordable medicines" has been implemented. This programme already provides outpatient care to patients with cardiovascular diseases, bronchial asthma and type 2 diabetes, who can receive medicines free of charge for a small surcharge based on a doctor's prescription. For the first 2 years, the "Affordable Medicines" reimbursement programme was administered by the Ministry of Health of Ukraine, and from 1 April 2019, the programme is administered by the National Health Service of Ukraine (NHSU). The list of medicines covered by the programme was approved by the Resolution of the Cabinet of Ministers of Ukraine No. 152 of 17 March 2017. Following the transfer of the administration of the programme to the National Health Service, medicines are dispensed only on electronic prescriptions (e-prescriptions), which were introduced on 1 April 2019. On 24 December 2020, the NHSU had contracts with 1216 legal entities and 8977 pharmacies are participating in the "Affordable Medi-

cines" Programme, of which 7576 have already dispensed medicines under the programme.^[12]

According to the NHSU, as of 3 August 2023, contracts were in place with 1,255 pharmacy businesses in 13,400 pharmacies, of which almost 9,600 pharmacies were dispensing medicines under the reimbursement scheme. According to statistics, during the six months of 2023, the doctors issued 1.18 million e-prescriptions per month, of which €24900 were paid to patients in pharmacies during the war. This means that the repayment rate is 83%. According to the results of the first half of 2023, NSHU paid out almost €45454546 to pharmacies, of which 23762263 EUR was allocated to insulins.^[13] In the Reimbursement List in force today, approved by the Order of the Minister of Health of 21 February 2023. No. 351, there are 486 trade names of medicines. The total budget of the reimbursement programme "Affordable medicines" for 2023 was € 118686689. Since October, 2023 23 names of test strips for diabetes were included in the Reimbursement list.^[18]

The Russian invasion, which commenced in 2022, has persisted for over two years. Despite the challenging conditions faced by Ukraine's healthcare and pharmaceutical supply system, the country's macroeconomic indicators at the end of the year exceeded initial expectations set at the onset of the full-scale conflict. However, military operations continue to have a significant impact on the development of Ukraine's economy and its entering pharmaceutical market. According to the 2022 results, the pharmaceutical market for retail sales of medicinal products showed a decrease of 6% compared to 2021, although at the beginning of the war in Ukraine a decrease of 17-29% was predicted. As for the forecasts for 2023, they are quite optimistic, with the volume of pharmaceutical sales in local currency expected to increase by 7% in the pessimistic scenario and by 30% in the optimistic scenario.^[14]

It is important to examine changes in the availability and affordability of oral glucose-lowering medicines (GLMs) for the treatment of T2D since the war in Ukraine. The aim of this work was to benchmark the availability and affordability of oral GLMs for the treatment of T2D prior to the Russian invasion in 2022 and 2023, in order to assess trends and prospects for the pharmaceutical supply of patients with T2D.

Research materials and methods:

The object of the research was information from the State Register of Medicinal Products (<http://www.drlz.com.ua>) and information on the presence of medicines and their

prices in the online pharmacy search engine (www.tabletki.ua, www.liki24.com) as of 20 May 2023 and 10 February 2022 (we use previous own data). The Anatomical Therapeutic Chemical (ATC) classification was used. The insulin preparations are also used in the treatment of diabetes, but were not included in the study. Marketing, analytical, graphical, generalisation analyses were used. Cost analysis of 1 Defined Daily Dose (DDD) due to the World Health Organisation (WHO) ATC/DDD ratio and solvency ratio analysis were used. The solvency ratio (Ca.s.) was determined by dividing the average retail price of medicines for a given period (month) by the average salary for the corresponding period (month).^[15]

Where:

Ca.s. - solvency ratio;

\bar{P} - average retail price of medicines for the relevant period;

Wa.w. - average salary/pension for the period.

Ca.s. - solvency ratio to be calculated.

Data from the State Statistical Service of Ukraine (<http://www.ukrstat.gov.ua>) on average salaries and pensions were used for the calculations. (EUR 390) <https://vikna.tv/dlia-tebe/ekonomiya/serednya-zarplata-v-ukrayini-2023-na-sogodni/>)

We also used our own data from 10 February 2022 and 20 May 2023.

Results

For the comparative analysis of group A10B - Blood glucose-lowering medicines, insulins, which according to the ATC classification are included in group A - Gastrointestinal system and metabolism (A10 - Drugs used in diabetes), were studied. Based on previous results of an analysis of the status of GLM registration in Ukraine before the war^[16], it was concluded that there was a sufficient list registered and actually available during the war to allow the use of modern treatment regimens for T2D, in accordance with the international guidelines.

A comparative analysis of the data in **Table 1** showed that there was little change in volumes over the study period February 2022 - May 2023. Thus, as at 20 May 2023, the marketing study showed that both quantitative and qualitative changes had occurred during this period. The assortment of medicines of group A10B - Hypoglycaemic medicines, excluding insulins, registered on the Ukrainian pharmaceutical market in 2023 amounted to 172 items, taking into account the amount of active substance in dosage form. Most of these were foreign-produced drugs - 113 trade names (65.7%) and 59 domestic-produced drugs. This means that the number of GLM

Table. 1 Glucose lowering medicines, excluding insulins (A10B), on the pharmaceutical market of Ukraine (2022- 2023)

International Non-proprietary Names	The number of registered GLMs by trade name							
	February2022				May2023			
	unit		in total		unit		in total	
	Foreign	Ukrainian	unit	%	Foreign	Ukrainian	unit	%
A10B A Biguanides								
Metformin	30	22	52	32.2	35	25	60	34.9
A10B B Sulfonylureas								
Glibenclamide	2	3	5	3.1	2	3	5	2.9
Gliquidone	1	-	1	0.6	1	=	1	0.6
Gliclazide	7	4	11	6.7	7	4	11	6.4
Glimepiride	24	15	39	24.1	22	12	34	19.7
A10B D Combinations of oral blood glucose lowering medicines								
Metformin/Glimepiride	1	2	3	1.9	1	3	4	2.3
Metformin/Glibenclamide	5	1	6	3.8	5	1	6	3.5
Metformin/Glipizide	1	-	1	0.6	1	-	1	0.6
Metformin/Gliclazide	1	-	1	0.6	1	-	1	0.6
Sitagliptin /Metformin	3	-	3	1.9	3	-	3	1.7
Vildagliptin /Metformin	3	2	5	3.1	5	2	7	4.0
Dapagliflozin / Metformin	3	-	3	1.9	3	-	3	1.7
Saxagliptin / Dapagliflozin	1	-	1	0.6	1	-	1	0.6
Saxagliptin / Metformin	-	-	-	-	2	-	2	1.2
<u>Empagliflozinum</u> /(Metformin	-	-	-	-	2	-	2	1.2
A10B F Alpha glucosidase inhibitors								
Voglibose	-	2	2	1.3	-	2	2	1.3
A10B G Thiazolidinediones								
Pioglitazone	-	3	3	1.9	-	3	3	1.7
A10B H Dipeptidyl peptidase) 4 DPP (4-inhibitors								
Sitagliptin	3	2	5	3.1	3	2	5	2.9
Vildagliptin	2	2	4	2.4	2	2	4	3.3
Saxagliptin	2	-	2	1.3	2	-	2	1.2
Linagliptin	1	-	1	0.6	1	-	1	0.6
Gemigliptin	1	-	1	0.6	-	-	-	-
A10B J Glucagon-like peptide) 1-GLP (1-analogues								
Liraglutide	2	-	2	1.3	2	-	2	1.2
Semaglutide					1	-	1	0.6
A10B K Sodium-glucose co-transporter) 2 SGLT2 (inhibitors								
Dapagliflozin	2	-	2	1.3	3	-	3	1.7
Empagliflozin	2	-	2	1.3	2	-	2	1.2
A10B X Other blood glucose lowering drugs .excl .insulins								
Repaglinide	6	-	6	3.8	6	-	6	3.5
	103	58	161	100	113	59	172	100

names increased by only 6.8% compared to the pre-war period. However, positive qualitative changes can be noted regarding the registered GLM list. Compared to 2023, the number of combinations increased from 8 INN combinations to 10 INN combinations.

Thus, the list of GLMs expanded to include the single-component Semaglutide and the two-component drugs: the combination of saxagliptin with metformin, empagliflozin with metformin. Another formulation, Dapagliflozin, and the combination drugs Wildagliptin with Metformin and Glimepiride with Metformin were also registered. There was a slight increase in the number of registered metformin drugs (foreign production) and a decrease in the number of glimepiride drugs. In 2023, the drug Gemigliptin will not be available. This means that it can be seen that, despite the war, the pharmaceutical supply system in Ukraine has recovered very quickly during the year and positive changes have taken place. New drugs from modern drug groups for the treatment of type 2 diabetes, such as glucagon-like peptide-1 (GLP-1) analogues and sodium-glucose cotransporter 2 inhibitors, became physically available. The expansion of the list was mainly at the expense of foreign drugs, which is due to the fact that the Ukrainian manufacturers do not produce modern GLMs from these groups.

The actual presence of GLMs in pharmacies in Ukraine was checked (realistic data as of 20.05.2023) from www.tabletki.ua, www.liki24.com. It was found that some registered GLMs are absent in pharmacies. The domestic drugs are present in a higher percentage (91%) than foreign drugs (51. %), which means that there is stability of treatment with appropriate drugs.

Compared to the pre-war period, the presence of domestic GLMs in pharmacies was 86% and foreign ones 48%. It should be noted that despite the registration of new drugs in 2022, some of them (Semaglutide, Semaglutide and Dapagliflozin) are not affordable for patients in 2023.

The cost of treatment with innovative drugs is self-funded by the patient. The prices of mono GLMs were investigated using the DDD method, the cost of DDD and their socio-economic availability based on the payment capacity adequacy factor for the two data. A comparative analysis of DDD values showed that the 4 GLMs presented in the pharmaceutical market of domestic and foreign production differ significantly from each other.

In this year (data from 10 February 2022 and 20 May 2023 were used) of martial law in Ukraine, the DDD cost of sulphonylurea derivative drugs and metformin hardly changed. The DDD cost of the drugs Vogliboz, Pioglitazone and Empagliflozin increased by 14%, 12% and 6.5%. For the other most expensive drugs, the DDD cost even

decreased by 2.1% - 6.7% compared to the pre-war period. The minimum DDD cost for mono GLD was found to be glibenclamide in 2023 (€0.025) and pre-war (€0.028). The maximum DDD cost for liraglutide was reduced in 2023 compared to 2022 from €2.29 to €2.23. Thus, during the period of martial law, pharmaceutical companies responded adequately by providing high-value medicines to patients (Table 2).

Table 2: Solvency rate of hypoglycaemic drugs for the treatment of T2D on the Ukrainian market in 2022-2023

International Non proprietary Names INN	DDD	Solvency adequacy ratio for the working population% .			
		2022		2023	
		Ukrainian	foreign	Ukrainian	foreign
Glibenclamide	10 mg	0.23	0.58	0.20	0.58
Metformin	2 g	0.62	1.54	0.62	1.55
Gliquidone	60 mg	-	2.2	-	2.30
Gliclazide	60 mg	0.31	0.80	0.39	0.49
Glimepiride	2 mg	0.62	0.82	0.58	0.82
Voglibose	0.6 mg	3.91	-	4.20	-
Pioglitazone	30 mg	2.57	-	2.71	-
Sitagliptin	0.1g	-	11.83	-	10.90
Vildagliptin	0.1 g	4.82	-	4.39	-
Saxagliptin	5 mg	-	7.49	-	5.10
Liraglutide	1.5 mg	-	18.67	-	17.13
Dapagliflozin	10 mg	-	6.50	-	6.02
Empagliflozin	17.5 mg	-	7.99	-	7.99
Repaglinide	4 mg	-	5.47	-	4.80

The Ca.s. ratio characterises the affordability of the drug and the possibility of selling it under conditions of low social solvency. In determining the solvency ratio of GLM's socio-economic affordability, the ratio of average salary and pension was adopted.

The calculated solvency ratio (Ca.s.) shows that a ratio below 1.0 ensures the affordability of the drug for the patient. The higher the value of the solvency ratio (Ca.s), the more expensive the medicines are for the patient and the less available for treatment.^[13] According to the calculated accessibility indices, GLMs were classified as very affordable (Ca.s.<5%); moderately affordable (5% < Ca.s. < 15%); not very affordable – Ca.s. > 15%.^[13]

Table 2 showed that the affordability of GLMs has not changed radically and that affordability of some GLMs has even increased. Most Ukrainian manufacturers and foreign drugs are very affordable, but foreign GLMs of innovative groups are moderately affordable. The likes of Liraglutide and Sitagliptin are difficult to access for the working population, given the calculated solvency adequacy ratio. However, the affordability of GLMs such as

glucagon-like peptide-1 (GLP-1) analogues and SGLT2 inhibitors is very important for reducing health complications in patients with diabetes.

According to the American Diabetes Association guidelines, glucagon-like peptide-1 (GLP-1) analogues and SGLT2 inhibitors are recommended in patients with cardiovascular and renal disease, patients with high risk of cardiovascular and renal complication.^[17]

The reimbursement register in force today in the "Affordable Medicines" programme, approved by the Decree of the Minister of Health of 21 February 2023. N 351, contains 486 trade names. There are only 3 core GLM medicines in this programme - glibenclamide, glibenclamide and metformin. The number of reimbursed GLMs has not changed during the war.^[13] It is imperative that innovative GLMs are included in the "Medicines for Affordability" reimbursement programme to ensure better affordability of innovations for diabetes patients and reduction of complications.

This study is based on data from before the war in Ukraine and now shows that the affordability and availability of GLMs during armed conflicts have not changed drastically. It was found that the list of registered medicines has been expanded. It can be assumed that the healthcare system in Ukraine is the strongest and provides stability in pharmaceutical supply for people with diabetes.

Conclusions:

1. Our study conducted between 2022 and 2023 showed that, despite martial law during this period, there were no significant changes in the system of pharmaceutical supply of GLMs to the Ukrainian population, thanks to the joint coordinated work of the Ministry of Health of Ukraine, manufacturers and pharmacies. The number of registered GLMs increased by only 6.8% compared to the pre-war period and amounted to 172 units.
2. During the war period, new drugs for the treatment of type 2 diabetes, such as glucagon-like peptide-1 (GLP-1) analogues and sodium-glucose cotransporter 2 inhibitors, as well as two combination drugs that were not available on the pharmaceutical market, became available on the market. The expansion of the product range was mainly at the expense of foreign-produced drugs.
3. In the year of martial law in Ukraine, it was established that the cost per DDD of sulphonylurea and metformin derivative drugs included in the reimbursement programme "Affordable medicines" practically did not change. In the case of some drugs (Vogli-

boz, Pioglitazone and Empagliflozin), the cost per 1 DDD increased by 14.0-6.5%. For the most expensive drug, the cost per DDD decreased by 2.1% - 6.7% compared to the pre-war period.

4. The affordability of GLM medicines has not changed radically due to the reimbursement programme "Affordable medicines", for some medicines it has even improved. Domestically produced drugs and foreign drugs are very affordable, but foreign GLMs of innovative groups are moderately affordable. Liraglutide and Sitagliptin are barely affordable for the working population, given the calculated solvency ratio.
5. Between 2017 and 2023, only three GLMs are issued as e-prescriptions and are compensated to T2D patients under the "Affordable Medicines" programme. Positively that since 2023, October was introduced into the reimbursement programme test strips for diabetes. It limits the access to the modern therapy for patients with diabetes. It is necessary to expand the list of GLMs in the reimbursement programme.

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