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CONTENT ANALYSIS OF THE RANGE OF ANTINEOPLASTIC DRUGS REGISTERED IN THE REPUBLIC OF UZBEKISTAN

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ABSTRACT

This article presents a comprehensive content analysis of antineoplastic drugs registered in the Republic of Uzbekistan between 2022 and 2024. Based on the The State Register of Medicines and medical devices and medical equipment approved for use in medical practice of the Republic of Uzbekistan (the State Register), the study focuses on pharmacotherapeutic groups L01, L02, L03, and L04 according to the ATC classification. The number of registered trade names, the proportion of imports, and domestic production were evaluated. Special attention was given to alkylating agents, antimetabolites, taxanes, antitumor antibiotics, and targeted therapies. The study identifies key international nonproprietary names with stable or declining registration dynamics and highlights gaps in the current pharmaceutical supply. Findings emphasize the country's reliance on foreign suppliers, especially for high-tech drugs, and suggest directions for localization and import substitution to strengthen pharmaceutical self-sufficiency.

Introduction: Oncological diseases are among the leading causes of mortality worldwide, including in Uzbekistan [1, 2]. One of the main ways to reduce cancer mortality is to provide access to effective and modern anti-cancer drugs [3, 4]. Therefore, it is important to analyze the range of anti-tumor drugs registered on the pharmaceutical market in Uzbekistan.

The content analysis of the State Registry allows us to assess the level of representation of different pharmacotherapeutic groups, track the dynamics of registration activities, and identify potential opportunities for import substitution and development of domestic pharmaceutical production. This analysis is particularly relevant in the context of Uzbekistan's policy to localize production of essential drugs and establish a sustainable supply chain [5, 7].

The aim of this study is to conduct a comprehensive analysis of antitumor medications registered in Uzbekistan between 2022 and 2024, classified according to the Anatomical, Therapeutic, Chemical (ATC) classification system. We will examine the quantitative and qualitative characteristics of the product range within groups L01, L02, L03, and L04.



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Additionally, we will identify the most popular international non-proprietary names (INNs) and propose areas for future domestic production [6].

Methodology: The official data from the State Register for 2022, 2023 and 2024 served as the main source of information for this study. The focus of the research was on medicines registered in Uzbekistan with anatomic, therapeutic, and chemical codes L01 (antitumor drugs), as well as related groups L02 (hormones and antagonists), L03 (immunostimulants), and L04 (immunosuppressants).

The study employed a content analysis approach to analyze the range of registered anticancer drugs, including:

- Systematizing registered medicines based on the ATC classification;
- Estimating the number of registered brand names by group, subgroup, and International Nonproprietary Name (INN);
 - Comparing registration data for three consecutive years (2022, 2023, and 2024);
 - Determining the proportion of domestic and imported medications in each category;
 - Identifying trends in product range changes and areas for local production development.

The data was analyzed using Microsoft Excel's tabular tools, including the creation of pivot tables and calculation of annual changes. The criteria for evaluation were the number of registered names, availability of domestic production, and presence of essential drugs in the registry.

Results. As part of the content analysis of the State Register for 2022, 2023, and 2024, data on the Anatomical, Therapeutic, Chemical Classification (ATC) system were analyzed, with a focus on Group L01 - "Antitumor Drugs". Special attention was paid to Subgroup L01A - Alkylating Drugs, which includes several international nonproprietary (INN) names, such as cyclophosphamide, chlorambucil, ifosfamide, and bendamustine.

During the period from 2022 to 2024, the pharmaceutical market in the Republic of Uzbekistan showed stability in terms of registration activity for this group. Specifically, cyclophosphamide (L01AA01), which is presented annually with three registrations (two from foreign sources and one from the CIS), has not seen the emergence of domestic analogues during this time. A similar pattern continues for ifosfamide (L01AA06), which has also been registered annually only by foreign manufacturers, with one registration per year.. It is worth noting that there are no registered dosage forms available for a number of international non-proprietary names (INNs), such as chlorambucil (L01AA02), melphalan (L01AA03), chloromethine (L01AA05), trophosfamide (L01AA07), prednimustine (L01AA08), busulfan (L01AB01), threosulfan (L01AB02) and thiotepa (L01AC01). This may indicate a low demand for these drugs or opportunities for expanding their availability when forming a state drug policy.

Against the background of the overall number of registered trade names, the L01A subgroup has a limited number of domestic products. For the entire analyzed period, there has not been a single domestic drug registered, indicating a potential opportunity for localizing production.

Bendamustine (L01AA09) showed a positive trend, with three registrations in 2024 after two in 2022 and 2023. All items were of imported origin. Temozolomide (L01AX03) also showed a steady presence with at least one domestic drug each year, making it an exception



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among the other alkylating compound group. This analysis of the L01A subgroup indicates a high dependence on imports and a lack of product range diversity. The lack of local production in this segment emphasizes the need for government support to encourage pharmaceutical companies to localize the production of these alkylating anti-cancer drugs.

In 2022, seven trade names were registered in this group. Among them, temozolomide (L01AX03) was the most common active ingredient, with three registrations (one domestic and two foreign). One drug was registered for cyclophosphamide (L01AA01), and ifosfamide (L01AA06) was also registered, both manufactured in CIS countries. Bendamustine (L01AA09) was represented by two trade names imported from other countries.

In 2023, the number of registered trade names remained the same at seven. At the same time, three drugs (including one domestic one) were newly registered for temozolomide. Cyclophosphamide and ifosfamide continued to be present in the registry as well. The number of bendamustine trade names remained unchanged, with two positions represented by foreign manufacturers.

By 2024, the range had expanded to eight registered names. Temozolomide continued to occupy a leading position, with three positions (one domestic, two foreign).. The number of registrations for bendamustine has increased to 3, indicating a growing interest in this drug. Cyclophosphamide and ifosfamide are still represented by one product each. Therefore, temozolomide (L01AX03) maintains the most stable position in the group, with at least one domestic product represented annually. This makes it a promising area for localization and production.

Table 1 provides data on the number of registered products in the L01A subgroup for 2022-2024.

Table 1.

The dynamics of the range of registered L01A group drugs in the Republic of Uzbekistan for the period from 2022 to 2024.

INN	ATC	2022	2023	2024
Temozolomide	L01AX03	3	3	3
Bendamustin	L01AA09	2	2	3
Cyclophosphamide	L01AA01	1	1	1
Ifosfamide	L01AA06	1	1	1
Other alkylating agents	_	0	0	0
Total	_	7	7	8

It is important to note that throughout the entire period, domestic production is represented only by temozolomide, the remaining items are completely imported from abroad or the CIS countries. This highlights the need to develop and implement import substitution programs in the segment of alkylating anticancer drugs.

The L01B group of Antimetabolites is represented by a wider range of international names compared to alkylating agents and plays a key role in the treatment of various malignancies. According to the results of the analysis of the State Register for 2022-2024, the range of drugs in this group demonstrates both stable and increasing trends in a number of active substances.



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The largest share in the group's structure is occupied by fluorouracil (L01BC02), the number of registrations of which increased from 4 in 2022 to 5 in 2024, while 1 drug of domestic production is registered annually. Gemcitabine (L01BC05) demonstrates consistently high representation – 3 names annually, of which 1 position belongs to domestic production.

Among the purine analogues, mercaptopurine (L01BB02) is registered annually for one item of foreign origin. Capecitabine (L01BC06) is also represented by one imported drug in each of the three analyzed years. For cytarabine (L01BC01), stability is observed – 2 positions annually, including 1 domestic registration.

Methotrexate (L01BA01) deserves special attention, demonstrating a steady presence on the market: 3 names annually, among which at least 1 domestic drug is presented each year.

The number of trade names for pemetrexed (L01BA04) is 2 annually, including 1 domestic drug in 2023 and 2024. The absence of registrations for the entire period is observed for such items as clofarabine (L01BB06) and pentastatin (L01BB03), which indicates a possible niche for expanding the range in the future.

Table 2 shows the dynamics of registered antimetabolites in Uzbekistan for 2022-2024. **Table 2.**

The dynamics of the range of registered medications in the L01B category in the Republic of Uzbekistan over the period 2022-2024.

INN	ATC	2022	2023	2024
Methotrexate	L01BA01	3	3	3
Pemetrexed	L01BA04	2	2	2
Mercaptopurine	L01BB02	1	1	1
Cytarabine	L01BC01	2	2	2
Fluorouracil	L01BC02	4	4	5
Gemcitabine	L01BC05	3	3	3
Capecitabine	L01BC06	1	1	1
Others		0	0	0
Total	_	16	16	17

The analysis showed that the antimetabolite group had the most balanced ratio of domestic and imported drugs, as well as stable registration activity over the past three years. Among these drugs, fluorouracil, methotrexate, and gemcitabine were of particular interest for local production. These drugs have a steady supply of domestic forms.

The L01C group included a wide range of natural and semi-synthetic anticancer agents. This group included periwinkle alkaloids, podophyllotoxin derivatives, taxanes, and other naturally occurring compounds. According to the State Register of Medicines of the Republic of Uzbekistan, this group demonstrated stable but moderate dynamics. A significant portion of the range was represented by foreign-manufactured products.

In the L01CA - Periwinkle Alkaloids and Their Analogues subgroup, Vinorelbine (L01CA04) was the most frequently registered drug, with two names each in 2022 and 2023 (including one drug produced in CIS countries), but there were no registrations in 2024. Other members of this subgroup, such as Vinblastine, Vincristine, Vindesine, and Vinflunine, were not registered during this time period.



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In the L01CB - Podophyllotoxin Derivatives subgroup, only Etoposide (L01CB01) was represented. It was registered five times in 2022, four times in 2023, and two times in 2024, all of which were imported drugs. This may suggest a gradual decline in interest in this drug or a focus on specific brand names.

The subgroup with the most prominent representation throughout all three years was L01CD - Taxanes. In particular:

- Paclitaxel (L01CD01) has an average of eight registrations per year, including three from CIS countries.
- Docetaxel (L01CD02) from 10 in 2022 to 9 in 2024, with 3-4 being produced in the Commonwealth of Independent States (CIS) countries.
 - Kabazitaxel (L01CD04) is represented by one imported drug each year.

Other drugs in this group, including colchicine derivatives (demecolcine) and those in the LO1CX subgroup, such as trabectedin, are not registered.

Therefore, the L01C category is characterized by a high number of registrations for taxa, but with almost no domestic production. This indicates significant reliance on external supplies, highlighting the potential for localizing at least one or two drugs, such as paclitaxel and docetaxel.

Table 3 shows the dynamics of the range of registered drugs in the L01C group in the Republic of Uzbekistan for the period 2022–2024.

Table 3.

The dynamics of the range of registered drugs in the L01C group in the Republic of Uzbekistan for the period 2022-2024

INN	ATC	2022	2023	2024
Vinorelbin	L01CA04	2	2	0
Etoposide	L01CB01	5	4	2
Paclitaxel	L01CD01	9	7	8
Docetaxel	L01CD02	10	10	9
Kabazitaxel	L01CD04	2	1	1
Total	_	28	24	20

During the period from 2022 to 2024, the number of registered names in this group has gradually decreased from 28 to 20, which requires special attention from regulatory authorities and manufacturers in order to ensure the availability of drugs in oncological practice.

The L01D group includes anticancer antibiotics and their derivatives that have a pronounced cytotoxic effect and are widely used in chemotherapy for various types of cancer. According to the State Register of Medicines in Uzbekistan for 2022-2024, there are a limited number of international generic names for drugs in this group, and registration activity has been declining.

Among the most widely used drugs in the group, doxorubicin (L01DB01) is the most prominent, with 6 registrations in 2022, 5 registrations in 2023, and 4 registrations in 2024. One of these positions is occupied by a domestic manufacturer each year, making it a key drug in the localization strategy for the L01D group.



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In 2022, epirubicin (L01DB03), a member of the anthracycline subgroup, was registered twice, once in 2023 and zero times in 2024. Daunorubicin (L01DB02), also from the anthracycline family, was only registered once in 2022 and was a drug from a foreign manufacturer. Idarubicin (L01DB06), another member of this subgroup, was also registered annually, but only once per year and exclusively from foreign sources.

Bleomycin (L01DC01) from the glycopeptide family was only registered in 2022. Mitomycin (L01DA03), on the other hand, was not registered in any of the analyzed years. This highlights the limited availability of certain drugs within this category.

Doxorubicin, therefore, bears the majority of the treatment burden, while other drugs in this category are either available sporadically or not at all. The lack of registration for several important international nonproprietary names (INN) points to potential gaps in cancer patient care and potential opportunities to expand the product range available to patients.

Table 4 shows the dynamics of the range of registered drugs in the L01D group in the Republic of Uzbekistan for 2022–2024.

Table 4.

Dynamics of the range of registered drugs of the L01D group in the Republic of Uzbekistan (2022-2024)

INN	ATC	2022	2023	2024
Doxorubicin	L01DB01	6	5	4
Epirubicin	L01DB03	2	1	0
Daunorubicin	L01DB02	1	0	0
Idarubicin	L01DB06	1	1	1
Bleomycin	L01DC01	1	0	0
Total		11	7	5

In general, the L01D group has seen a reduction in the number of registered trade names, from 11 in 2022 to 5 in 2024. This indicates a need to review approaches to the registration of vital antitumor antibiotics and stimulate their localization, especially for products with high clinical significance.

The L01X group includes a wide range of anticancer agents that are not included in other categories of the ATX classification. These include targeted drugs, monoclonal antibodies, and other innovative molecules. These products are characterized by their high cost, specific purpose, and limited availability. This is reflected in their registration activity in Uzbekistan.

According to data from the State Registry for 2022-2024, the most commonly registered drugs in this category are:

- Bortezomib (L01XX32): 2-3 different registered names each year. One of these is produced domestically, making it a unique example of localization within this group of drugs.
- \bullet Rituximab (L01XC02) 2 names per year, all produced by CIS countries or foreign companies.
 - Bevacizumab (L01XC07) 2-3 names, exclusively imported. A stable presence is also observed for:
 - Trastuzumab (L01XC03) 2-3 registrations per year, with no domestic analogues.



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Immunotherapeutic drugs such as nivolumab (L01XC24), pembrolizumab (L01XC18), and carmustine (L01AD01), are registered as individual items, exclusively from imported origins.

Some drugs, such as sorfenib (L01XE05) and sunitinib (L01XE04), have been registered under 1-2 different names each, with variations from year to year. The new innovative molecule lasertinib (L01XE63) was only added to the registry in 2024, indicating a gradual expansion in the range of modern targeted therapies available.

Special attention should be given to the increase in the number of registered drugs in the L01XE subgroup, which includes tyrosine kinase inhibitors. In 2022, there were 6 names of these drugs, in 2023 - 7, and in 2024 - 10. These include afatinib, lanvatinib, and erlotinib. However, all of these drugs are imported and no domestic analogues have been registered in this subgroup.

Table 5 shows the dynamics of the range of registered drugs in the L01X group in the Republic of Uzbekistan for 2022–2024.

Table 5.

Dynamics of the range of registered drugs of the L01X group in the Republic of Uzbekistan (2022-2024)

INN	ATC	2022	2023	2024
Bortezomib	L01XX32	3	2	3
Rituximab	L01XC02	2	2	2
Bevacizumab	L01XC07	2	2	3
Trastuzumab	L01XC03	2	3	2
Sunitinib	L01XE04	1	1	1
Sorafenib	L01XE05	1	1	1
Afatinib, lasertinib, etc.	L01XE*	6	7	10
Nivolumab, pembrolizumab	L01XC18/24	1	1	2
Others	_	4	5	6
Total	_	22	24	30

Thus, the L01X group demonstrates the most intensive growth dynamics: the total number of registered drugs increased from 22 in 2022 to 30 in 2024. However, at the same time, there is practically no domestic production, with the exception of single positions on bortezomib. This indicates the need for strategic import substitution measures in the segment of high-tech anticancer drugs and the expansion of local production of targeted and biological therapies.

The L02 group includes drugs used for hormone–dependent tumors, in particular, breast cancer, prostate cancer, etc. According to the results of the analysis of the State Register for 2022-2024, the range of drugs in this group demonstrates relative stability and moderate representation, with the dominance of foreign and CIS-made products.

Letrozole (L02BG04) is the most widely represented – 3 names in 2022 and 2023, 4 in 2024, while 1 drug of domestic production is registered annually. A similar situation is observed for tamoxifen (L02BA01) – 2-3 names per year, of which 1 domestic drug is present in each of the years.



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Among the analogues of gonadotropin-releasing hormone (GnRH), buserelin (L02AE01) is represented by one registration annually, all drugs are imported. Anastrozole (L02BG03) – 2 drugs each year, and exemestane (L02BG06) – 1 drug each in 2023-2024 were also consistently registered.

In 2024, there are new registrations for enzalutamide (L02BB04) and abiroterone (L02BX03), which indicates a gradual expansion of the range of modern antiandrogens on the Uzbek market.

Table 6 shows the dynamics of the range of registered drugs in the L02 group in the Republic of Uzbekistan during 2022–2024.

Table 6.

The dynamics of the range of registered drugs in the L02 group in the Republic of Uzbekistan during 2022-2024

INN	ATC	2022	2023	2024
Tamoxifen	L02BA01	3	2	2
Letrozole	L02BG04	3	3	4
Anastrozole	L02BG03	2	2	2
Exemestan	L02BG06	0	1	1
Buserelin	L02AE01	1	1	1
Enzalutamide	L02BB04	0	0	1
Abiroterone	L02BX03	0	0	1
Total	_	9	9	12

Thus, the drugs in the L02 group show a gradual increase in range, especially due to the inclusion of modern hormone blockers. Local production is partially represented by letrozole and tamoxifen.

The L03 group includes drugs used for both cancer treatment and the restoration of the immune system during chemotherapy, despite its common name. The content analysis shows that the most relevant drugs in oncology are lenograstim (L03AA13) and filgrastim (L03AA02).

Filgrastim (L03AA02) has been registered annually in the amount of three names, with at least one domestic drug being presented each year. Lenograstim (L03AA13) has been registered in 2022 with two drugs, 2023 with one, and 2024 without any.

Morphologically active interferons and interleukins have also been registered, but they are mostly not focused on oncological indications and are represented by a single item.

Table 7 shows the dynamics of the range of registered drugs in the L03 group in the Republic of Uzbekistan for 2022-2024.

Table 7.

The dynamics of the range of registered drugs in the L03 group in Uzbekistan (2022-2024)

INN	ATC	2022	2023	2024
Filgrastim	L03AA02	3	3	3
Lenograstim	L03AA13	2	1	0
Interleukins, etc.	L03AC*	1	1	1
Total	_	6	5	4



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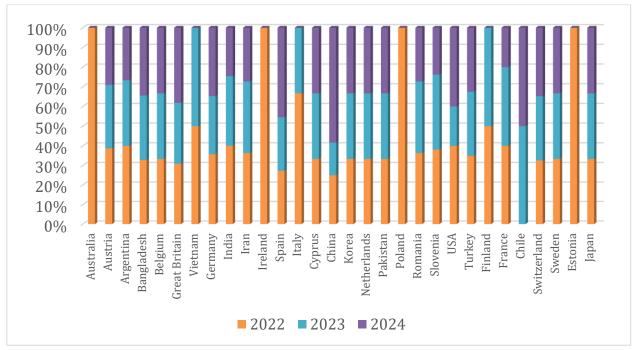
Against the backdrop of a limited number of international brands, the L03 group stands out for its high proportion of domestically produced products, particularly in the case of fillgrastim. This indicates the successful implementation of an import substitution policy within this group.

The L04 group, which was originally intended for the treatment of transplantation and autoimmune diseases, also includes drugs used for immunosuppression in oncohematological pathologies. Specifically, these include rituximab (L01XC02), which is classified in some sources under L04AA, as well as other drugs such as alemtuzumab (L04AA34).

According to the analysis of registration data, 1-2 immunosuppressive drugs with oncological indications are registered annually, but their classification in the database is primarily attributed to the L01X group, not the L04 group. Therefore, there are virtually no oncological drugs registered in the L04 category, and the majority of these drugs are classified in other ATX categories. This leads to the conclusion that, within the context of this analysis, the L04 group is of limited significance and is not considered a major segment of antitumor therapy in Uzbekistan.

Figure 1 shows the distribution dynamics of registered drugs produced by foreign countries for the years 2022, 2023, and 2024, represented as a percentage of the total for each country.

Figure 1. The distribution dynamics of registered drugs produced by foreign countries



In 2022-2024, there was a steady registration of foreign-made medicines in Uzbekistan. The largest number of registered drugs in this category was from India, with 109 registered in 2022, 96 in 2023, and 67 in 2024. The number of Indian drugs registered remains the highest, although there is a downward trend that may indicate market saturation or stricter registration requirements.



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Regarding German-made drugs, the figures were as follows: 34 in 2022, 33 in 2023, and also 33 in 2024. These registration figures have been relatively stable for three years. There has been a slight increase in registered positions, with drugs from Switzerland maintaining a consistent presence in the market, with 15, 16, and 16 registered in 2022, 2023, and 2024 respectively.

Other countries, such as the USA, Turkey, France, China, and Japan, have fewer registered drugs but demonstrate stable or slightly varying participation in the domestic pharmaceutical system.

Figure 2 shows the number of registered drugs produced in CIS countries for the years 2022, 2023, and 2024.

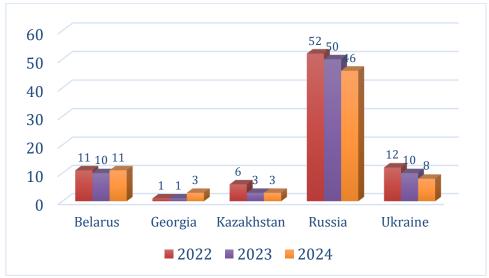


Figure 2. The number of registered drugs produced in CIS countries

- The number of registered Russian drugs in Uzbekistan has decreased from 52 in 2022 to 46 in 2024. The trend for Ukrainian drugs has also shown a decrease, with 12 in 2022, 10 in 2023, and 8 in 2024.
- In contrast, Belarus, Georgia, and Kazakhstan have a relatively low and stable presence in the Uzbek pharmaceutical market, with rates ranging from 1 to 11 registered drugs per year.

This indicates that while the number of drugs from these countries may be small, they are still present in the market and have maintained a consistent level of availability.

Figure 3 shows the number of registered local drugs in Uzbekistan for the years 2022, 2023, and 2024.

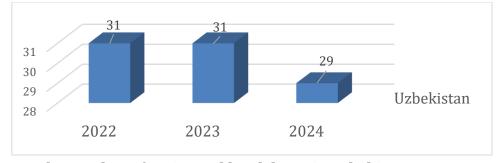


Figure 3. The number of registered local drugs in Uzbekistan



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 \bullet The following number of domestic drugs were included in the State Register: in 2022 – 31, in 2023 – 31, in 2024 – 29.

The share of domestic pharmaceuticals remains stable, which could indicate a well-established manufacturing sector. However, there was a slight decrease in 2024, which requires further investigation (possibly due to temporary, regulatory, or technological factors). The highest number of drug registrations in 2022 went to India, followed by Germany, Switzerland, and Russia. In 2023, India continued to lead with 109 registrations, but by 2024, this figure had dropped to 67. This may be due to several factors, including stricter regulatory requirements, the saturation of the market with generic drugs, and the growth of local production in India. Registrations of Russian drugs also decreased from 52 in 2022 to 46 in 2024. This could be attributed to geopolitical instability, logistical challenges, competition from Asian and European manufacturers, and the implementation of import substitution policies in Uzbekistan. The number of registered drugs from Uzbekistan remained relatively stable at around 29-31 per year, indicating the presence of production facilities and government support for local industries. However, a decrease in registrations in 2024 suggests the need for additional incentives such as tax incentives, grants, and simplification of regulatory procedures to encourage further growth.

Conclusions. Thus, the pharmaceutical market in Uzbekistan in 2022-2024 is characterized by a stable registration of both foreign and domestic medicines, with a clear dominance of products from India and Russia. However, there are also signs of transformation, such as reducing dependence on certain countries and gradually increasing local production. The further development of the pharmaceutical industry requires a balanced government policy that stimulates national producers and ensures a wide geographical diversity of imported medicines.

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