

Analysis of the retail range of antifungal medicines using an integrated ABC-XYZ analysis matrix

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ABSTRACT

The work aims to conduct an ABC-XYZ analysis with the creation of an integrated matrix to obtain an idea of the place of each drug of the triazole derivatives group in the assortment of pharmaceutical organizations, as well as the structure of their application and the assessment of their contribution to the commodity circulation. Antifungal drug market (1,432 drugs presented), ABC analysis, XYZ analysis, statistical analysis, comparative analysis, content analysis, graphical method. The research showed a wide prevalence of triazole derivatives in the antimycotic drug market (360 drugs, 26%). Furthermore, ABC - and XYZ-analyses of the representatives of this group were carried out. The results of these analyses were used to construct an integrated ABC-XYZ matrix. In the resulting matrix, all antimycotics represented by triazole derivatives were divided into 9 groups, each of which is characterized by its contribution to the range of antifungal drugs, their turnover, the level of consumer value, the reliability of forecasting, and the tendency to seasonal fluctuations. Retail and wholesale participants in the pharmaceutical market should always review the range of different medicines in connection with the rapid development of modern pharmacotherapy. The group of antimycotics that are triazole derivatives continues to develop rapidly. The research shows that at the moment these medicines occupy a leading place in the Russian pharmaceutical market. With the help of ABC and XYZ analyses, an integrated matrix was compiled that allows pharmaceutical organizations to evaluate and adjust the range of antifungal drugs that are triazole derivatives.

Keywords: Antifungal drugs, Triazole derivatives, ABC analysis, XYZ analysis, Integrated matrix of ABC-XYZ analyses, Pareto chart

Introduction

Fungal diseases (mycoses) are an important medical and social problem of modern society [1, 2]. In addition to superficial mycoses, when the lesion in most cases affects the nail plates, systemic mycoses that affect vital organs and systems are becoming more widespread. Every year, more than 1.5 million

people become victims of fungal diseases. According to the latest global estimates, 3000000 cases of chronic pulmonary aspergillosis, 223100 cases of cryptococcal meningitis, 700000 cases of invasive candidiasis ending in severe candida sepsis are registered annually. No less severe mycotic infections, such as pneumocystis pneumonia, affect about 500,000 people annually, invasive aspergillosis and disseminated histoplasmosis-250,000 and 3100,000 people, respectively [3, 4]. The average annual incidence of lethal mycotic infections in the Russian Federation is 11,840 cases of candidiasis, 3,238 cases of invasive aspergillosis, and 52,311 cases of chronic lung aspergillosis [5]. Various factors contribute to such a rapid spread of mycoses. So, some surface infections are quite trivial, for example, mycosis of the feet and hands, however, invasive systemic mycoses occur in patients with immunodeficiency conditions caused by the use of glucocorticoids, antitumor, and immunosuppressive drugs. Immunodeficiency conditions also

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occur in the presence of HIV infection and after transplantation of internal organs and tissues. In addition, the number of patients with tuberculosis has recently increased, which is also a significant risk factor for fungal infection [6-8].

Currently, the pharmaceutical market is rich in various medicines, which are both mono- and multicomponent, and recently combined. The search for new pharmacologically active molecules with antifungal activity is carried out, which is associated with the optimization of the general profile of patients (age group, pregnancy), with a decrease in toxicity (especially for systemic antimycotics), as well as the spectrum of antifungal action [9-11]. Among modern antifungal drugs, an important place is occupied by azoles, which have been used since the second half of the 20th century [10]. This group includes imidazoles and triazoles, the mechanism of action of which is to inhibit the enzyme 14- α -sterol demethylase, which leads to a violation of the construction of the cell wall of fungi [12]. However, better tolerability and less serious side effects should be noted in representatives of triazoles used in the treatment of systemic mycoses (Fungal meningitis, cryptococcosis, systemic candidiasis, aspergillosis) [10, 13]. There are 2-generation triazoles, among which we can distinguish relatively new voriconazole, structurally similar to fluconazole, but with a wider spectrum of action, including against fungi resistant to fluconazole [14]. Among the newer representatives of the 2nd generation, isavuconazole can be distinguished, under the spectrum of action of which yeast (genera *Candida*, *Cryptococcus*, etc.), mycelial fungi (genera *Aspergillus*, including strains resistant to amphotericin B and even to echinocandins), dimorphic fungi (*Histoplasma capsulatum*, *Coccidioides* spp., *Blastomyces dermatitidis*) fall [15, 16]. Clinical trials have also shown that isavuconazole is not inferior to voriconazole in invasive aspergillosis, alternative therapy for the emergency treatment of mucormycosis, and is suitable for the treatment of invasive candidiasis [14, 17].

Due to the wide distribution and introduction of new triazole derivatives into clinical practice, it is important to study the range of this group in the modern Russian pharmaceutical market. In this research, we used the marketing methods of analysis – ABC and XYZ, with the further creation of an integrated matrix that allows us to get an idea of the place of each drug of the analyzed group in the assortment of pharmaceutical organizations, their contribution to the turnover and an idea of the structure of the use of these antifungal drugs. Such a matrix will help to adjust the existing modern range of antifungal medicines for pharmaceutical organizations.

Materials and Methods

Materials

The Russian pharmaceutical market of antifungal medicines are represented by 1432 drugs.

Methods: ABC analysis, XYZ analysis, statistical analysis, comparative analysis, content analysis, graphical method.

In this article, we studied the annual reports of analytical agencies for the research of the Russian pharmaceutical market of antifungal drugs for 2019. Based on these data, the drugs were grouped according to the chemical structure of the active substances, where the most widely represented group on the Russian pharmaceutical market was identified. Then ABC - and XYZ-analyses of this group were carried out with further construction of the integrated ABC-XYZ matrix.

ABC analysis is a method of resource research, which consists of dividing the assortment of products into categories A, B, and C, which make up 80, 10, and 10% of the sales structure (in physical and price terms), respectively. This principle is called the Pareto principle, according to which 20% of the effort provides 80% of the result. As a result, each category formed by the ABC method has its characteristics: category A includes the most valuable goods for the organization that provides maximum sales and are constantly in the assortment, category B includes goods that provide a stable volume of sales for the organization, category C includes goods that make the least contribution to assortment sales, since they practically do not bring income [18, 19]. Thus, it is possible to identify the most valuable products for the retail segment of the pharmaceutical market, identify representatives who are "outsiders" in the commercial assortment of the studied group of medicines, as well as identify drugs that form the inventory of pharmaceutical organizations. During the ABC analysis, the trade names assigned to each drug by the manufacturers were used (without taking into account the different dosage forms, the specific brand of the manufacturer was taken into account). Based on the calculation of the total sales amount for 2019 (taking into account all quarters) (wholesale price in rubles), antifungal medicines were sorted in descending order, followed by the division of each specific commercial drug into groups A, B, and C based on the calculated cumulative contribution. The results of the analysis were visualized on the Pareto chart.

In turn, XYZ analysis allows you to analyze and predict the stability of certain business processes (business objects). For example, you can use it to determine the predictability of the behavior of different groups of customers or the stability of sales of certain types of goods. During the XYZ analysis, the coefficient of variation was calculated, then the drugs were grouped into three categories: category X – a group of products that are characterized by stable sales or consumption and high forecasting capabilities (the value of the coefficient of variation is in the range 0-10%), category Y – a group of products characterized by seasonal fluctuations and average forecasting capabilities (the value of the coefficient of variation is in the range of 10-25%), category Z is a group of products with irregular consumption, that is, there are difficulties in identifying trends, and low forecasting accuracy is characteristic (the value of the coefficient of variation is above 25%) [19, 20]. Next, an integrated ABC/XYZ analysis matrix was constructed, which allows us to get an idea of the place of each drug of the analyzed group in the assortment of pharmaceutical organizations, as well as to assess their contribution to the turnover and get an idea of the structure of use [21]. Such a

matrix will help to adjust the existing modern range of antifungal drugs that are triazole derivatives for pharmaceutical organizations.

Microsoft Excel 2019 software was used for all types of analysis. Using this program, real-value distribution graphs, a Pareto chart, and an integrated ABC-XYZ matrix were constructed.

Results and Discussion

The modern pharmaceutical market is characterized by a steady growth of new medicines, the range of which is replenished, including due to the entry of combined drugs into the market. It is worth noting that currently a large number of generic drugs are registered, which have different trade names with the same active substances.

Previously, it was shown that today there are 1,432 antifungal drugs on the Russian pharmaceutical market, with the main market share being occupied by fluconazole - 22% and terbinafine – 16 % [22].

In the course of the research, all the analyzed antifungal drugs were grouped based on the chemical structure of the active substances (**Figure 1**). Combined drugs containing 2 or 3 active substances were assigned to the chemical group of the main therapeutically active component, or isolated separately if the combined drug did not contain a true antifungal agent (for example, antiseptics, broad-spectrum antibiotics, etc.). Triazole derivatives (3rd generation antimycotics) are the largest group represented by 360 drugs (26%). Next in the number of drugs are imidazole derivatives (antimycotics of the 2nd generation) 260 drugs (18%) and allylamines 213 drugs (15%). Among the truly antifungal active substances, the drug Griseofulvin accounts for only 3 drugs (in the total structure of the assortment, slightly more than 0%). A relatively large number of herbal medicines (117-8%), which is almost equal to the number of polyenes (119-8%). Thus, triazole derivatives occupy the first place in the structure of the assortment on the Russian pharmaceutical market.

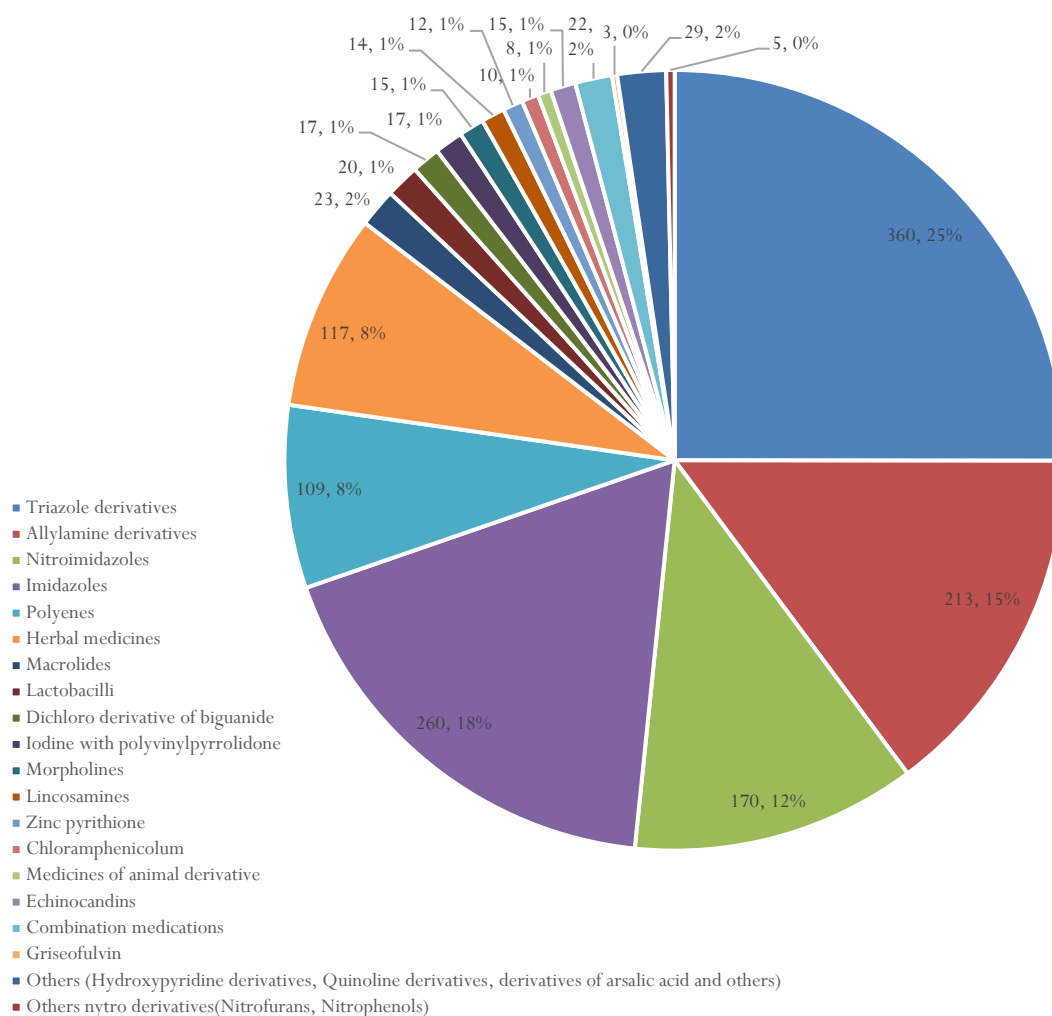


Figure 1. The range of antifungal medicines grouped by chemical structure (the quantities of medicines and the share of their group from the total number are indicated)

ABC-analysis was used to analyze and identify the most priority positions of individual antimycotic drugs of the triazole derivatives group in the assortment of the modern Russian

pharmaceutical market. For clarity, a Pareto chart with group subdivisions is built (Figure 2).

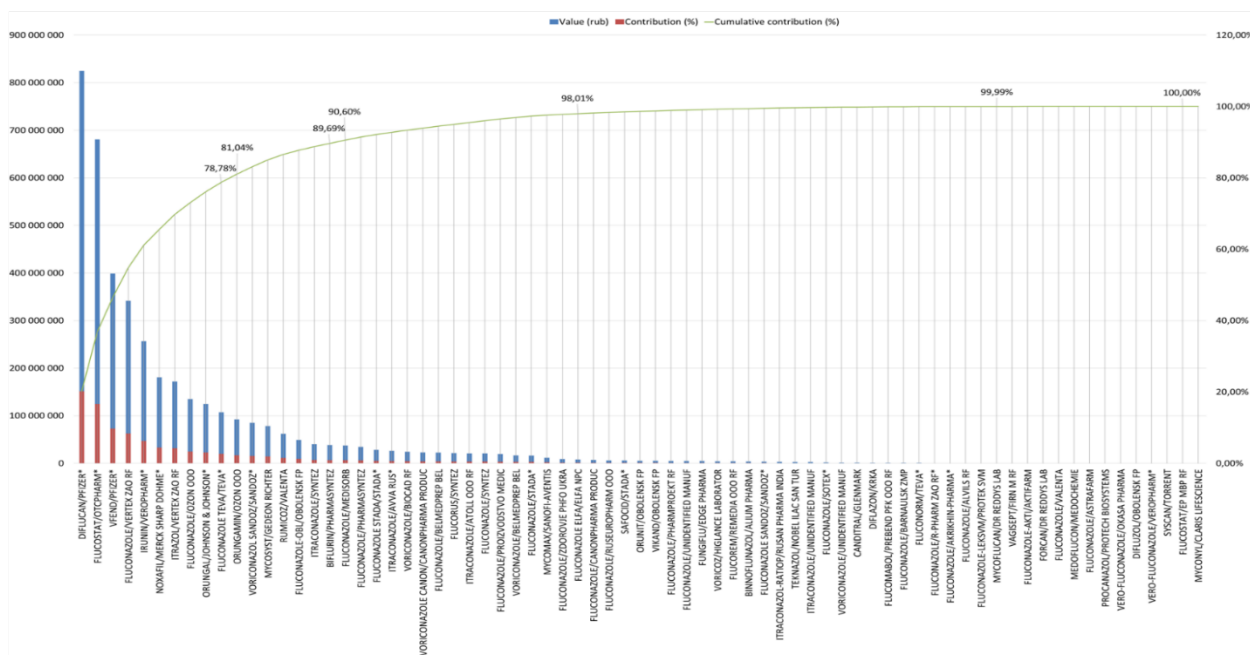


Figure 2. Pareto chart based on the results of ABC analysis of antifungal drugs

All drugs belonging to group A, and above all the leaders of this group, among which we can distinguish Diflucan («Pfizer»), Flucostat («OTCpharm» JSC), Vifend («Pfizer»), Fluconazole («Vertex» JSC) and Irunin («Veropharm» JSC), should always be present in the assortment of retail and wholesale participants of the Russian pharmaceutical market since they ensure maximum sales among drugs that are derivatives of triazole. The influence of all representatives of group A on the turnover of antifungal medicines is the greatest, so pharmacy organizations need to take this group of products into account first.

Group B drugs are «average» in importance in the range of antimycotics of the triazole derivatives group. These include Orungamin (LLC «Ozon»), Voriconazole Sandoz («Sandoz»), Mycosist (JSC «Gedeon Richter»), Rumycos («Valenta Pharm»), Fluconazole-OBL (JSC «OBL Pharm»), Itraconazole (JSC «Synthez») and Biflurin (JSC «Pharmsynthez»). All of these drugs provide a stable sales volume, so investments from various market participants should be directed to maintaining the current level of sales of these antimycotics. In Group C, 18 representatives can be identified, with a share of up to 0.01% in the total contribution - these are the drugs Fluconazole (JSC R-Pharm, JSC Akrikhin, Alvis, Valenta, Astrapharm), Fluconazole-LEKSVIM (LLC PROTEK-SVM), Mycoflucan («Dr. Reddy's Laboratories»), Vagisept (LLC FIRN M), Forcan («Dr. Reddy's Laboratories»), Fluconazole-Akti (LLC «Aktipharm»), Medoflucon («MEDOCHEMIE»), Procanazole («PROTECH BIOSYSTEMS»), Vero-Fluconazole (JSC «Veropharm»), Difluzol (JSC «OBL Pharm»), Vero-Fluconazole («Okasa Pharma»), Syscan («Torrent pharmaceuticals»), Flucostat (EP MBP RF), Myconil («Claris

LiveScience»). These drugs are «outsiders» among the triazole derivatives on the market since their contribution to total sales is minimal to 0.01% or equal to 0. In this regard, it is advisable to remove the above drugs from the range of antifungal drugs. The ABC analysis reflected the contribution of various antifungal drugs of the triazole derivatives group to the assortment of the Russian pharmaceutical market, as well as the impact on the turnover of pharmacies of various forms of ownership, but they cannot assess the frequency of purchase and seasonal fluctuations in demand. To do this, an XYZ analysis was performed. The coefficient of variation was calculated using the formula:

$$v = \sqrt{\frac{\sum_{i=1}^n (xi - \bar{x})^2}{n}} \cdot 100\% \tag{1}$$

where v - is the coefficient of variation, xi - is the value of the parameter for the evaluated object for the i-th period, x - is the average value of the parameter for the evaluated object of analysis, n - is the number of periods. Further, based on the value of the obtained coefficients of variation of each drug (in%), the drugs were grouped into 3 groups: group X: 0-10%, group Y: 10-25%, group Z: over 25%. For clarity, a diagram of the distribution of all representatives of the triazole group (in percentage and quantitative terms) is constructed (Figure 3). Most of the drugs considered were classified as category Z.

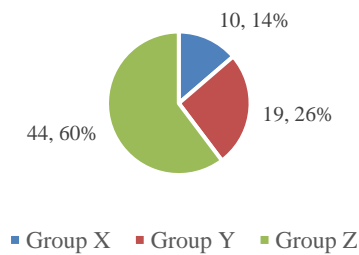


Figure 3. Distribution of antifungal drugs based on the results of the XYZ analysis

During the research, an integrated matrix was compiled based on the results of ABC/XYZ analyses with the distribution of drugs into 9 categories: AX, AY, AZ, BX, BY, BZ, CX, CY, and CZ (**Table 1**).

Table 1. Matrix projection of the integrated ABC and XYZ analysis of the largest group of antifungal drugs on the domestic pharmaceutical market

ABC/XYZ	X	Y	Z
A	5-7% "care and cherish" Flucostat (JSC «OTCpharm»), Fluconazole (JSC «Vertex»), Itraconazole (JSC «Vertex»), Fluconazole (LLC «Ozon»)	5-7% "take care and work" Diflucan («Pfizer»), Irunit («Veropharm» JSC), Orungal («Johnson & Johnson» LLC), Fluconazole Teva (Teva Pharmaceutical Industries)	10-12% "watch carefully" Vfend («Pfizer»), Noxafil (Merck Sharp&Dohme)
	6-8% "love and grow" Mycosist (JSC «Gedeon Richter»)	15-17% "think and analyze" Orungamin (Ozon LLC), Rumycos (Valenta Pharm JSC), Itraconazole (Synthet OJSC)	15-17% "leave it to yourself" Voriconazole Sandoz (Sandoz), Fluconazole-OBL (JSC Pharmaceutical Enterprise «OBL Pharm»), Biflurin (JSC «Pharmsynthez»)
B	10-12% "calm down and wait" Fluconazole (JSC «Medisorb»), Fluconazole STADA (JSC «Nizhpharm»), Mycomax (JSC «Sanofi Russia»), Forcan («Dr Reddy's Laboratories»), Medofluron («Medochemie»)	10-12% "provide himself" Fluconazole (JSC «Pharmsynthez»), Itraconazole (LLC «Atoll»), Fluconazole («POLPHARMA»), Terazol (Nobel ILAC Sanayi ve Ticaret), Itraconazole (LLC «Lekpharm»), Candidal («Glenmark Pharmaceuticals»), Diflazon (JSC «KRKA, D. D., Novo mesto»), Fluconazole (LLC «PFK Prebends»), Fluconazole (JSC «Synthet»), Fluconazole (JSC «Canonpharma production»), Fluconazole (LLC «Pharmaceutical company «Health»), Fluconazole (JSC "Scientific-production center "ELFA")	15-20% "get rid of immediately" Itraconazole (JSC «Abba Rus»), Voriconazole (JSC «Biocad»), Voriconazole (JSC «Canonpharma Production»), Fluconazole (JSC «Belmedpreparaty»), Voriconazole (JSC «Belmedpreparaty»), Flucorus (JSC «Synthet»), Fluconazole (LLC «Production of medicines»), Fluconazole (LLC «Rusoro pharm»), Safocid (JSC «Nizhpharm»), Orunit (JSC «OBL Pharm»), Vikand (JSC «OBL Pharm»), Fluconazole (JSC «Pharmproekt»), Fungiflu (Edge Pharma), Voricoz (Higlance laboratoris), Fluorem (LLC «Remedia»), Binnoflunazole (JSC «Alium»), Fluconazole Sandoz (Sandoz), Itraconazole Ratiopharm (Rusan India), Fluconazole (Sotex) Voriconazole (LLC «Atoll»), Fluconazole (LLC «Barnaul factory of medicines»), Fluconorm (Teva Pharmaceutical Industries), Fluconazole (CJSC «R-Pharm»), Fluconazole (JSC «Akrikhin»), Fluconazole («Alvis»), Fluconazole («Valenta»), Fluconazole («Astrapharm»), Fluconazole (LEKSVM LLC «PROTEK-SVM»), Mycoflucan («Dr. Reddy's Laboratories»), Vagisept (FIRN M LLC), Fluconazole-Acti (Aktipharm LLC), Procanazole (PROTECH BIOSYSTEMS), Vero-Fluconazole (Veropharm JSC), Difluzol (JSC OBL Pharm), Vero-Fluconazole (Okasa Pharma), Syscan (Torrent pharmaceuticals), Flucostat (EP MBP RF), Myconil (Claris livescience)
	C		

Based on the obtained matrix projection of the integrated ABC/XYZ analysis, the following conclusions can be drawn:

1. Medicines of the AH and BX groups: have a high degree of forecasting, stable sales, high (AX group "care and cherish"), and medium (BX group "love and grow") consumer value. These antifungal medicines should always be present in the assortment of pharmaceutical enterprises, both wholesale and retail because they provide a high turnover and stability of sales, and their consumption is stable and predicted with a high degree of accuracy.
2. Medicines of the groups AU and BY: have a high (AY "care and work") and average (BY "think and analyze") consumer value, average reliability of the forecast, and is characterized by seasonal fluctuations. For these antifungal

drugs, it is necessary to create a significant stock, since they are characterized by instability of consumption, which, in turn, requires constant availability in the assortment of pharmaceutical organizations.

3. Medicines of the AZ and BZ groups: have a high (AZ "watch closely") and medium (BZ "provide yourself") consumer value, a fairly low degree of forecasting reliability due to stochastic consumption (that is, it reaches more than 50% monthly, weekly predictability is less than 70%). For drugs of this group, it is necessary to optimize sales in the market. Optimization can be achieved, for example, by assigning individual managers in a pharmaceutical company responsible for these groups

(applicable to both retail and wholesale participants in the pharmaceutical market).

4. Medicines of the CX group ("calm down and wait"): they have a low consumer value, a high degree of forecasting due to the stability of consumption. For medicines of this group, it is advisable to reduce inventory in warehouses and use a system with a constant order period.
5. Medicines of the CY group ("provide yourself"): have a low consumer cost, average reliability of the forecast due to the instability of consumption. The drugs of this group have a predisposition to seasonal fluctuations, in this regard, it is necessary to form a stock of goods in the warehouse due to unstable consumption in different quarters of the year.
6. Medicines of the CZ group ("get rid of immediately"): have a low consumer cost, low reliability of forecasting due to stochastic consumption. A large number of the analyzed triazole derivatives fell into this group, but the decision to withdraw from the range of antifungal drugs, first of all, should be implemented for products with the lowest share in the total contribution (up to 0.01% according to ABC analysis) and with the highest coefficient of variation (90-200%). The remaining part of the group should be subject to strict control and monitoring by pharmaceutical organizations.

Thus, as a result of the ABC-XYZ analyses conducted with the further compilation of the integrated matrix, it was found that the best antifungal drugs among triazole derivatives from the point of view of the assortment policy of pharmaceutical organizations are the drugs Flucostat (JSC "OTCpharm"), Fluconazole (JSC "Vertex"), Itrazole (JSC "Vertex"), Fluconazole (LLC "Ozon"), while a large number of drugs currently on the market fall under the category "get rid of immediately», what should be taken into account by various representatives of the wholesale and retail level of the pharmaceutical market.

Conclusion

Currently, the risk of fungal diseases is still high. This is especially true for systemic mycoses that affect vital organs and often cause death. The development of new antifungal agents and the rational use of existing drugs is a priority for medical and pharmaceutical specialists.

Some of the modern antifungal drugs related to triazole derivatives are quite promising from a pharmacological point of view (selectivity of action, good tolerability, and fewer adverse reactions). The research showed that these drugs are also the most widely represented group of antimycotics on the Russian pharmaceutical market.

ABC and XYZ analyses of triazole derivatives were performed with further integration of the results obtained in the form of an ABC-XYZ matrix and an evaluation of the drugs of the resulting categories. The resulting matrix will optimize the range of this group of antifungal medicines, which will have a positive

influence on the turnover and sales of pharmaceutical organizations.

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