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RESULTS OF RETROSPECTIVE ANALYSIS OF REGISTRATION OF ANTITUBERCULOSIS DRUGS AND THEIR PRESENCE IN STATE FORMULARY LIST IN UKRAINE

The results of a retrospective analysis of the domestic pharmaceutical market of antituberculiosis drugs are present in the article. Particular structural assessment of specified segment of the pharmaceutical market by the total quantity taking into account features of tuberculiosis therapy (drugs of the I and II ranges) in the dynamics of years and by the parameter "domestic / imported" had carried out. The author also presents the results of the study of antituberculiosis drugs available in five issues of the State Formulary List (for 2009-2013) and gives calculated share of domestic drugs in the general structure of antituberculiosis drugs listed in State Formulary List depending on the line therapy.

Key words: pharmaceutical market, antituberculosis drugs, registration of drugs, formulary list, retrospective analysis.

FORMULATION OF THE PROBLEM

Tuberculosis (TB) is one of the most actual problems for the national health system. Officially World Health Organization announced tuberculosis epidemic in Ukraine in 1995. The highest indexes of incidence of tuberculosis in Ukraine reached in 2005, when the rate increased three times compared to period till 2005(about 100 cases per 100 thousand of population). According to the available data of State Authority "Ukrainian center of control of socially dangerous diseases of Ministry of Health of Ukraine» in 2012 incidence had tended to modest growth rate of index – 1.3% compared with 2011 (from 67.2 per 100 thousand of pop. to 68.1 per 100 thousand of pop.).

According to the World Health Organization in Ukraine multirezystent tuberculosis have 16% of patients who first diagnosed, and 44% of patients with recurrence of TB [2, 10-12].

According to the literature, the value of TB treatment is high, and the process cannot be stopped (termination of therapy for more than 10 days - leading to the drug resistance to Mycobacterium). Nowadays there is chemotherapy resistance of pathogen to major anti-TB drugs (ATBD). The above necessitates the use of effective ATBD to treat TB patients under conditions of pharmacoeconomic study. In Ukraine an important role in providing of effective therapy is given to formulary system. Formulary system allows to carry out efficient and proper implementation of rational and cost-effective drug therapy that provides efficient use of funds for the purchase of drugs [33]. The specified range of measures intended to improve the quality of pharmaceutical care provided to the population, in particular its privileged categories

ANALYSIS OF RECENT RESEARCH AND PUBLICATIONS

Analysis of specialized literature of domestic authors revealed that a big weight is given to the quality of the existing anti-TB therapy, reducing of resistance to treatment and to the new approaches to drug therapy of tuberculosis. At the same time, current research on the analysis of the domestic pharmaceutical market of ATBD and a lists of anti-TB drugs listed in the State Formulary list for years 2009-2013 are missing.

FORMULATION OF PURPOSE OF THE ARTICLE

Analysis of pharmaceutical market has a key role in complex assessment of quality of pharmaceutical providing. Thereby retrospective analysis of domestic market of ATBD has been conducted, particular data of ATBD registration have been

analyzed. Also results of estimation of appearance of ATBD in State Formulary lists (I-V issue) have been shown.

PRESENTATION OF THE MAIN MATERIAL

According to the State Formulary drugs (5th issue) it is distinguished anti-TB drugs of I and II ranges [8]. ATBD of the I range are the main anti-TB drugs and are to prescribed to patients with newly diagnosed tuberculosis and recurrence of the disease, which emit sensitive Micobacterium tuberculosis (I-III categories of patients). These include: isoniazid, rifampicin, streptomycin, ethambutol, pyrazinamide, ryfapentyn, rifabutin, ftivazid. ATBD of the I range are reserved, they are used only in personalized / individual chemotherapy regimens in patients with IV category tuberculosis, which determine drug resistance to ATBD of the I range, as well as other categories of patients with resistance to Mycobacterium tuberculosis to ATBD of the I range or bad their portability. ATBD of the II range - kanamycin, amikacin, ethionamidum, protionamid, sodium aminosalitsylat, capreomycin, cycloserine, teryzydon, klofazymin.

Comparative analysis of registration data (November 2011 - April 2014) of anti-TB drugs according INN is presented in Table 1.

According to the State Register of drugs it is found that as of January 2014 in Ukraine 250 trade names of ATBD (including dosages) for 24 INN (including combined) from manufacturers from 15 countries were registered [3].

A comparative analysis of registered by trade names drugs to treat tuberculosis had shown that compared to 2011 the number of registered drugs in 2014 almost unchanged, with the exception of

Table 1

COMPARATIVE ANALYSIS OF REGISTRATION OF ANTI-TB DRUGS ACCORDING INN (2011 – 2014 YEARS)

Code ATC	INN January 2011	Quantity of registered trade names (including dosage)		The share of total, %	
		January 2014	January 2011	January 2014	
Anti-TB Drugs Of The I Range					
J04A C01	Isoniazid	10	23	4,04	9,2
J04A B02	Rifampicin	16	15	6,45	6,0
J01G A01	Streptomycin	2	2	0,8	0,8
J04A K02	Ethambutol	11	14	4,44	5,6
J04A K01	Pyrazinamide	10	12	4,04	4,8
J04A B05	Ryfapentyn	4	4	1,61	1,6
J04A B04	Rifabutin	6	4	2,42	1,6
J04A C03	Ftivazid	1	1	0,4	0,4
Total		60	75	24,2	30
Anti-TB Drugs Of The II Range and combined drugs*					
J01GB04	Kanamycin	1	1	0,4	0,4
J01GB06	Amikacin	20	19	8,06	7,6
J01DE01	Cefipim + amikacin	1	1	0,4	0,4
J04AD03	Ethionamidum	3	2	1,21	0,8
J04AD01	Protionamid	7	6	2,82	2,4
J04AA02	Sodium aminosalitsylat	6	12	2,42	4,8
J04AB30	Capreomycin	4	3	1,61	1,2
J04AB01	Cycloserine	5	5	2,02	2,0
J04AK03	Teryzydon	4	7	1,61	2,8
J04BA01	Klofazymin	8	2	3,23	0,8
J01MA01	Ofloxacin	38	28	15,32	11,2
J01MA16	Gatifloxacin	21	23	8,47	9,2
J01MA02	Ciprofloxacin	60	58	24,2	23,2
J01MA03	Pefloksacin	6	4	2,42	1,6
J01MA09	Sparfloxacin	3	3	1,21	1,2
J01RA04	*Gatifloxacin + ornidazole	1	1	0,4	0,4
Total		188	175	75,8	70,0
In all		248	250	100	100

several drugs, such as isoniazid, sodium aminosalitsylat, teryzydon, klofazymin, ofloxacin. It is founded that the largest share belong to ATBD of the II range (188 drugs of the total number of registered trade names in 2011 and 175 drugs in 2014, or 75.8% and 70.0% of the total respectively). Largest part of sample are fluoroquinolones (ATC code - J01MA) 52.02% and 46.8% of the total number of registered drugs in 2011 and 2014 respectively).

In accordance with the objectives of the study, we have analyzed the registered ATBD of the parameter 'domestic/foreign production". It is established, as of January 2014 the vast majority of ATBD meet India production drugs (122 drug names) and second place was taken by Ukraine (85 drugs). Value of trade name anti-TB drugs domestically is 34% and foreign production - 66%. Consequently, the share of imported ATBD in 2014 was significant.

WHO recommends that a comprehensive conceptual approach to rational drug therapy includes: providing of medical and pharmaceutical workers with provable, objective and independent information about drugs. So, on the initiative of the Ministry of Health of Ukraine to integrate into the European space State Formulary List of Drugs was carried out using WHO recommendations.

The next stage of our research was analysis of the State Formulary List of Drugs for the period from 2009 to 2013. Results of the structural analysis of ATBD in the State Formulary Lists of Drugs by INN are shown in the table 2.

As the table shows, significant changes in the dynamics and the presence of ATBD of the I range was not observe during analysed period. Such drugs as streptomycin and ftivazid, have not changed in any of the 5 issues of the State Formulary List; ryfatsyna and fenazyd were excluded from the State Formulary List from 2011 and 2010 years respectivly. Trends in direct increasing or decreasing of the number of registered ATBD presented in the State Formulary List was not observed [4-8].

As for ATBD of the II range, it should be noted that significant changes in the dynamics of the presence of a quantity of drugs had such ATBD of the II range as kanamycin, ethionamidum, klofazymin and gatifloxacin - reducing of the number of drugs, sodium aminosalitsylat, teryzydon and ofloxacin - increasing the number of drugs; capreomycin in general has not changed in any of the 5 issues of the State Formulary List [4-8].

To perform research tasks unified clinical protocols of treatment for TB patients were processed in the study. As a result, it was founded that the document does not include drugs such as ryfapentyn, ftivazid, ryfatsyn and fenazyd.

Next stage of study had included the analysis of the State Formulary List by the parameter "country of manufacture" of ATBD. Drugs of Indian production had taken the majority, ATBD of domestic production (by Ukrainian producers) had had second place. This findings correspond to the previously established tendency in the analysis of the registration of ATBD.

Value of trade names of drugs to treat tuberculosis of foreign and domestic production in 2014 had increased on more than 10% compared 2009, that is positive tendency (Fig.).

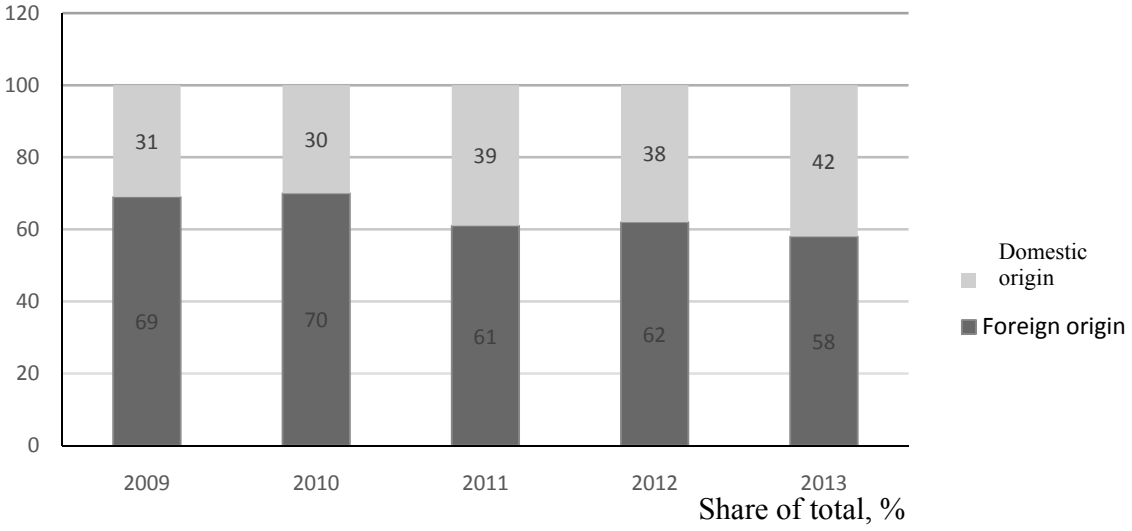

Figure. Value *of ATBD (by trade names) of foreign and domestic production presented in State Formulary Lists in 2009-2013*

Table 2

RESULTS OF THE STRUCTURAL ANALYSIS OF ATBD IN THE STATE FORMULARY LISTS OF DRUGS BY INN (PERIOD: 2009 – 2013YEARS)

Code ATC	INN	Year									
		2009		2010		2011		2012		2013	
		Quantity of drugs	Proportion, %	Quantity of drugs	Proportion, %	Quantity of drugs	Proportion, %	Quantity of drugs	Proportion, %	Quantity of drugs	Proportion, %
Anti-TB Drugs Of The I Range											
J04A C01	Isoniazid	5	3,57	5	4,04	5	3,53	5	3,65	4	3,39
J04A B02	Rifampicin	8	5,71	8	6,45	8	5,63	7	5,11	8	6,78
J01G A01	Streptomycin	1	0,71	1	0,8	1	0,7	1	0,73	1	0,85
J04A K02	Ethambutol	10	7,14	9	7,26	9	6,34	10	7,3	7	5,93
J04A K01	Pyrazinamide	8	5,71	7	5,65	8	5,63	8	5,84	7	5,93
J04A B05	Ryfapentyn	4	2,87	3	2,42	2	1,41	4	2,92	3	2,54
J04A B04	Rifabutin	7	5,0	5	4,04	6	4,23	6	4,38	5	4,24
J04A C03	Ftivazid	1	0,71	1	0,8	1	0,7	1	0,73	1	0,85
J04AB02	Ryfacyna	1	0,71	1	0,8	-	-	-	-	-	-
J04AC	Fenazyd	1	0,71	-	-	-	-	-	-	-	-
Total		46	32,84	40	32,26	40	28,17	42	30,66	36	30,51
Anti-TB Drugs Of The II Range											
J01GB04	Kanamycinum	3	2,14	2	1,61	2	1,41	1	0,73	1	0,85
J01GB06	Amikacin	10	7,14	7	5,65	9	6,34	8	5,84	8	6,78
J04AD03	Ethionamidum	5	3,57	2	1,61	3	2,11	3	2,19	2	1,69
J04AD01	Protionamid	5	3,57	4	3,23	6	4,23	6	4,38	4	3,39
J04AA02	Sodium aminosalitsylat	5	3,57	5	4,04	7	4,93	8	5,84	7	5,93
J04AB30	Capreomycin	4	2,87	4	3,23	4	2,82	4	2,92	4	3,39
J04AB01	Cycloserine	5	3,57	3	2,42	4	2,82	5	3,65	4	3,39
J04AK03	Teryzydon	1	0,71	1	0,8	3	2,11	3	2,19	4	3,39
J04BA01	Klofazymin	4	2,87	3	2,42	2	1,41	2	1,46	1	0,85
J01MA01	Ofloxacin	19	13,57	18	14,52	24	16,9	22	16,05	24	20,33
J01MA16	Gatifloxacin	15	10,71	15	12,1	18	12,68	13	9,49	12	10,17
Total		76	54,29	64	51,63	82	57,76	75	54,74	71	60,16
Combined Anti-TB Drugs											
J04AM02	Rifampicin + isoniazid + ethambutol	4	2,87	4	3,23	4	2,82	4	2,92	2	1,69
J04AM06	Rifampicin + isoniazid + pyrazinamide + ethambutol	7	5,0	7	5,65	7	4,93	7	5,11	4	3,39
J04AM	Isoniazid + ethambutol	1	0,71	1	0,8	1	0,7	1	0,73	-	-
J04AM	Sodium paraaminosalitsylat + isoniazid	1	0,71	1	0,8	1	0,7	1	0,73	1	0,85
J04AM02	Rifampicin + isoniazid	4	2,87	4	3,23	4	2,82	4	2,92	1	0,85
J04AB02	Rifampicin + pyridoxine	1	0,71	1	0,8	1	0,7	1	0,73	1	0,85
J01DE01	Cefepime + amikacin	-	-	1	0,8	1	0,7	1	0,73	1	0,85
J01RA04	Gatifloxacin + ornidazole	-	-	1	0,8	1	0,7	1	0,73	1	0,85
Total		18	12,87	20	16,11	20	14,07	20	14,6	11	9,33
In all		140		124		142		137		118	

Thus the State Formulary List of anti-TB drugs characterized by dependence on foreign products in 2009-2013 that had had negatively affect to the economic accessibility of pharmaceutical care for patients with tuberculosis. In the same time, on February 15, 2013 a legislative norm was introduced according to which all drugs imported into the territory of Ukraine have to be made in accordance with the standards of GMP. Therefore, in 2013 sharply reduced the number of Indian production' drugs.

Summarizing it should be noted that in the State Formulary List according to 2009-2013 al-

most unchanged the quantity of trade names of anti-TB drugs of foreign origin, with the exception of 2013. The quantity of trade names of anti-TB drugs of domestic production had increased in 2011-2013 compared with 2009-2010 that is a positive tendency from socio-economic point of view.

Thus in the study a retrospective analysis of anti-TB drugs registered in the domestic pharmaceutical market in 2014 compared to the 2011 was shown and the presence of anti-TB drugs in the State Formulary Lists during 2009-2013 years was assessed.

CONCLUSIONS AND PERSPECTIVES OF FUTURE INVESTIGATIONS

1. According to the State Register of drugs its found that as of January 2014 250 trade names PTLZ (including dosages forms) for 24 INN (including combined) from manufacturers from 15 countries were registered in Ukraine.

2. Analysis of the data of the State registration of drugs showed that the largest share had imported drugs, which in 2014 up 66.8%. Value of domestically ATBD by trade names was 33.2% respectively.

3. Analysis of registered ATBD revealed that during the study period the number of reported anti-TB drug almost unchanged with the exception of several drugs such as isoniazid, sodium aminosalitsylat, teryzydon, klofazymin, ofloxacin.

4. For an analysis of State Formulary Lists for the period from 2009 to 2013, it was concluded that significant changes in the dynamics of ATBD of the I rang were not observed. As for ATBD of the II range, it should be noted that significant changes in the dynamics had kanamycin, ethionamidum, klofazymin, gatifloxacin, sodium aminosalitsylat, teryzydon, ofloxacin and capreomycin.

5. Value trade names of drugs to treat tuberculosis of foreign and domestic production for 2009 is 69 and 31 %, respectively, in 2010 — 70% and 30% by 2011 — 61% and 39% by 2012 — 62% and 38% by 2013 — 58 % and 42 Consequently, in 2009-2013 ATBD listed in State Formulary List were characterized by dependence on foreign manufacturer.

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РЕЗУЛЬТАТИ РЕТРОСПЕКТИВНОГО АНАЛІЗУ РЕЄСТРАЦІЇ ПРОТИТУБЕРКУЛЬОЗНИХ ПРЕПАРАТІВ ТА ЇХ НАЯВНОСТІ У ДЕРЖАВНОМУ ФОРМУЛЯРІ В УКРАЇНІ

У статті представлено результати ретроспективного аналізу вітчизняного ринку протитуберкульозних препаратів. Зокрема, у динаміці років здійснено структурну оцінку вказаного сегменту фармацевтичного ринку за кількістю препаратів із урахуванням особливостей терапії туберкульозу (препарати I та II ряду), а також проведено аналіз за параметром «вітчизняний/ імпортний». Автором наведено результати вивчення наявності протитуберкульозних препаратів у п'яти випусках Державного формуляру (за 2009 - 2013 роки) та розраховано питому вагу протитуберкульозних ЛЗ вітчизняного виробництва у загальній сукупності протитуберкульозних препаратів, представлених у Державних формулярах залежно від лінії терапії.

Ключові слова: фармацевтичний ринок, протитуберкульозні препарати, реєстрація ЛЗ, формулярний перелік (формуляр), ретроспективний аналіз.

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РЕЗУЛЬТАТЫ РЕТРОСПЕКТИВНОГО АНАЛИЗА РЕГИСТРАЦИИ ПРОТИВОТУБЕРКУЛЕЗНЫХ ПРЕПАРАТОВ И ИХ НАЛИЧИЯ В ГОСУДАРСТВЕННОМ ФОРМУЛЯРЕ В УКРАИНЕ

В статье представлены результаты ретроспективного анализа отечественного рынка противотуберкулезных препаратов. В частности, в динамике лет осуществлена структурная оценка указанного сегмента фармацевтического рынка по количеству препаратов с учетом особенностей терапии туберкулеза (препараты I и II ряда), а также проведен анализ по параметру «отечественный /импортный». Автором приведены результаты изучения наличия противотуберкулезных препаратов в пяти выпусках Государственного формуляра (за 2009 - 2013 годы) и рассчитан удельный вес противотуберкулезных ЛС отечественного производства в общей совокупности противотуберкулезных препаратов, представленных в Государственных формулярах в зависимости от линии терапии.

Ключевые слова: фармацевтический рынок, противотуберкулезные препараты, регистрация ЛС, формулярный перечень (формуляр), ретроспективный анализ.

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