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- ВЫБОР ТЕХНОЛОГИИ СРАВНЕНИЯ ПРИ ПРОВЕДЕНИИ ФАРМАКОЭКОНОМИЧЕСКОГО АНАЛИЗА ИННОВАЦИОННЫХ ЛЕКАРСТВЕННЫХ ПРЕПАРАТОВ
- РЕЗУЛЬТАТЫ РОССИЙСКИХ ФАРМАКОЭКОНОМИЧЕСКИХ ИССЛЕДОВАНИЙ

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SELECTION OF A COMPARISON TECHNOLOGY FOR PHARMACOECONOMIC ANALYSIS OF INNOVATIVE DRUGS

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Summary: *This publication discusses the problem of choosing a comparison technology for pharmacoeconomic analysis. The relevance of this issue stems from the fact that the pharmacoeconomic analysis is based on a comparative competitive approach and that the comparison technology sets the point of reference and determines the sensitivity of the assessment. Pharmacoeconomic assessment is most needed for innovative drugs. In this context, the choice of comparison technology predetermines the results of the pharmacoeconomic evaluation of an innovative drug. The traditional approach used in choosing a comparison technology in a pharmacoeconomic analysis based on the evidence of medical use between the drug being investigated and the comparison technology has some limitations, especially when the drug of a new class is evaluated. In this case, the comparison technology often uses long-running medications, which are not comparable with the innovative drug, either in terms of efficiency (usually to a large extent) or at the cost of an innovative drug, which is often more high-priced. In these circumstances, the results of the pharmacoeconomic assessment of innovative drug will possibly be negative. The negative results may be a sign of not likely unacceptability of an innovative drug but the consequence of the incorrect choice of comparison technology, which sets the level of sensitivity of the pharmacoeconomic analysis, in which the innovation drug is known to be beyond its borders. For a solution to the situation, the authors suggest an alternative approach to the choice of comparison technology in the pharmacoeconomic analysis.*

Keywords: *pharmacoeconomics, clinic-economic analysis, innovative medicine, comparison technology, "golden standard" of treatment, "cost-efficiency" analysis, "budget impact" analysis.*

The development of the methodology of the major types of pharmacoeconomic analysis provides an opportunity to considerate the issue of selection of pharmacoeconomic valuation items.

The pharmacoeconomic analysis implies a competitive comparative approach, and there is a problem of choosing a comparison technology for the pharmacoeconomic evaluation of the drug. An analysis of practical experience with pharmacoeconomics shows [1-12, 16-27] that the following options are traditionally chosen as comparison technologies:

- historical control (palliative therapy or best available therapy);
- The "Golden standard" of treatment;
- A drug of a similar class;
- A drug of another class with similar indications for use;
- Innovative drug of another class with the same indications for use.

The list appears to be in line with possible alternatives to the choice of comparison technologies for drug clinical trials. This is because the pharmacoeconomic analysis takes into account the clinical efficiency of the drug under investigation, which is mostly derived from clinical trials. However, differences in the goals, objectives and methodology of clinical and pharmacoeconomic research lead to different results in the use of the same comparison technologies in assessing clinical and pharmacoeconomic efficiency. The wide range of options available for use complicates the problem of selecting the comparison technology in pharmacoeconomic analysis: the use of the indirect comparison methodology in pharmacoeconomic analysis makes it possible to use almost any of the above options as a comparison technology. It is important to note, that the selected comparison technology in the pharmacoeconomic analysis is the reference point in the pharmacoeconomic evaluation coordinate system, thus defining the initial analysis conditions and directly influencing the resulting pharmacoeconomic conclusion.

This article examines the conditions for selecting different comparison technologies from the perspective of various stakeholders in the pharmacoeconomic analysis, the particulars and limitations of their use, and the impact on the results of the pharmacoeconomic study.

As noted earlier, the main criterion in the traditional approach to the choice of comparison technologies in the pharmacoeconomic study is the clinical aspect-the conformity of the medical evidence of the drug and of the comparison technology. According to this principle, all possible options for comparison technologies can be ranked by the degree of reasonableness.

The existing international recommendations [30] on pharmacoeconomic analysis consider the preferred scenario of using as a technology a comparison of the most commonly accepted therapy, a "golden standard".

The choice of the "golden standard" of treatment in the role of comparison technology makes it possible to avoid criticizing the pharmacoeconomic research design. For example, from a clinical perspective, the use of the "golden standard" of treatment is reasonable, as it seems to be the best accepted practice. For decision makers, the use of the "golden standard" of treatment as a technology of comparison is also characterized by a high degree of persuasiveness, since in the vast majority of cases the drug/services of the "golden standard" of treatment are already included in the reimbursable listings, the results of the pharmacoeconomic research will demonstrate how the innovative drug would affect the actual efficiency of the distribution of resources in system of medicine provision. The choice of other options as comparison technologies if there is a current "golden standard" of treatment for the medical evidence in question may raise additional questions and the justifications for the target audience, which is presented with the results of the pharmacoeconomic analysis.

In the absence of a "golden standard" of treatment, the number of possible comparison technologies in the pharmacoeconomic analysis is increasing. Based on the principle of a general indication for use, next drug following the

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"golden standard"" of treatment may be the drug of the same pharmacological group or class and it may be chosen as the basis for comparison. The choice of a specific INN for comparison in the pharmacoeconomic study is, in fact, determined by the position of the drug in the pharmaceutical market (taking into account the prevalence of the use of drug in actual clinical practice, the presence or absence of drug in the lists, the competitive environment, etc.).

In a situation where an innovative drug of a new Class (group) is subject to a pharmacoeconomic assessment, the drug of other pharmacological classes (groups) with a similar statement of application may be used as comparison technologies. However, it is important to note that the comparison drugs can be selected from both the group of innovative classes and traditional ones. For example, when conducting a pharmacoeconomic analysis of innovative oncological drug belonging to the class of monoclonal antibodies, as a comparison technology, if there is no existing "golden standard" of therapy or other drug monoclonal antibodies in the treatment of the nosology in question, the drug of inhibitor of tyrosine kinases (innovative class of drugs) or one of the traditional chemotherapy schemes of cytotoxic drugs can be used. It should be noted that this situation does not negate the need to justify the selection of a specific drug chosen for the role of comparison technology in the pharmacoeconomic analysis.

If a new revolutionary drug is subject for pharmacoeconomic analysis, and it is used to treat a disease for which there was no prior effective therapy, the only available option as a comparison technology is historical control or better available/supportive/palliative therapy.

This traditional approach to the choice of comparison technology in the pharmacoeconomic study, based on indications for medical use, seems to be a clear and understanding for problem of pharmacoeconomic evaluation by clinical specialists. However, it is important to note that the pharmacoeconomic analysis is a tool for decision-making in the system of medicine provision. Its purpose is not to choose the optimum drug for patient treatment (this choice is within the competence of the attending physician, who defines the treatment tactics and the drugs based on the characteristics of the individual patient, his indications and contra indications, possible drug interactions, side effects of therapy, the treatment protocols and clinical recommendations) and, in general, the optimal use of the limited resources available to the health system in order to obtain the most effectiveness expressed by the increase in health per unit of resources. In this regard, an alternative approach to the selection of comparison technologies in the pharmacoeconomic assessment is becoming possible. However, before considering this approach, it is necessary to analyze how the selection of a comparison technology influences the results of the pharmacoeconomic assessment. It is proposed to study this issue in a consistent manner for two main types of pharmacoeconomic analysis: "cost-efficiency" and "budget impact".

The "cost-efficiency" analysis methodology involves calculating the value of the cost-efficiency coefficient (CER) for the investigational drug and comparison drug[13]. The specified coefficient reflects the cost per unit of efficiency at each of the drug: the cost-efficiency analysis actually determines the profitability of the drug. The calculation is based on efficiency and cost data (see formula (1)).

$$CER = Cost/Ef, \text{ where:} \qquad \text{Formula (1)}$$

CER - value of cost-efficiency coefficient, RUB;
Cost – Drug costs, RUB;
Ef – the value of drug effectiveness in the appropriate performance test.

The final phase of "cost-efficiency" analysis involves interpreting the resulting CER values. The investigational drug is regarded as the dominant from the pharmacoeconomic "cost-efficiency" analysis, provided that it is clinically more efficient drug comparisons, and that the CER values are less than for comparisons. If a clinically more effective drug is characterized by a larger CER, it is necessary to calculate the incremental ratio of "cost-efficiency" (ICER) with formula (2).

$$ICER = Cost(1) - Cost(2)/Ef(1) - Ef(2), \text{ where:} \qquad \text{Formula (2)}$$

ICER-value of an coefficient of "cost-efficiency", RUB
Cost(1) – Costs for drug 1, RUB;
Cost(1) – Costs for drug 2, RUB;
Ef (1) – the effectiveness of drug 1 in the appropriate performance test.
Ef (2) – the effectiveness of drug 1 in the appropriate performance test.

The obtained value is compared with [1] c "willingness to pay" (WTP), which can be defined as three per capita GDP per annum. If the value of ICER below the WTP, the "cost-efficiency" conclusion of a clinically more effective drug is formulated. In a situation where the calculated ICER is above the WTP, it may be possible to raise the issue of the inadmissibility of a clinically more effective drug for the health system and its financial capacities. Thus, the comparison technology has a direct impact on the resulting pharmacoeconomic conclusion, based on the competitive nature of the "cost-efficiency" analysis. To illustrate this impact more clearly, imagine two hypothetical situations: a pharmacoeconomic evaluation of the innovative drug X in the treatment of the M disease. In the first case, the reference technology is the routinely outdated treatment of the M disease, and in the second case is used another innovative drug is used (table 1). The relevant base values and the calculation of "cost-efficiency" analysis for proposed hypothetical situations are also presented in table 1.

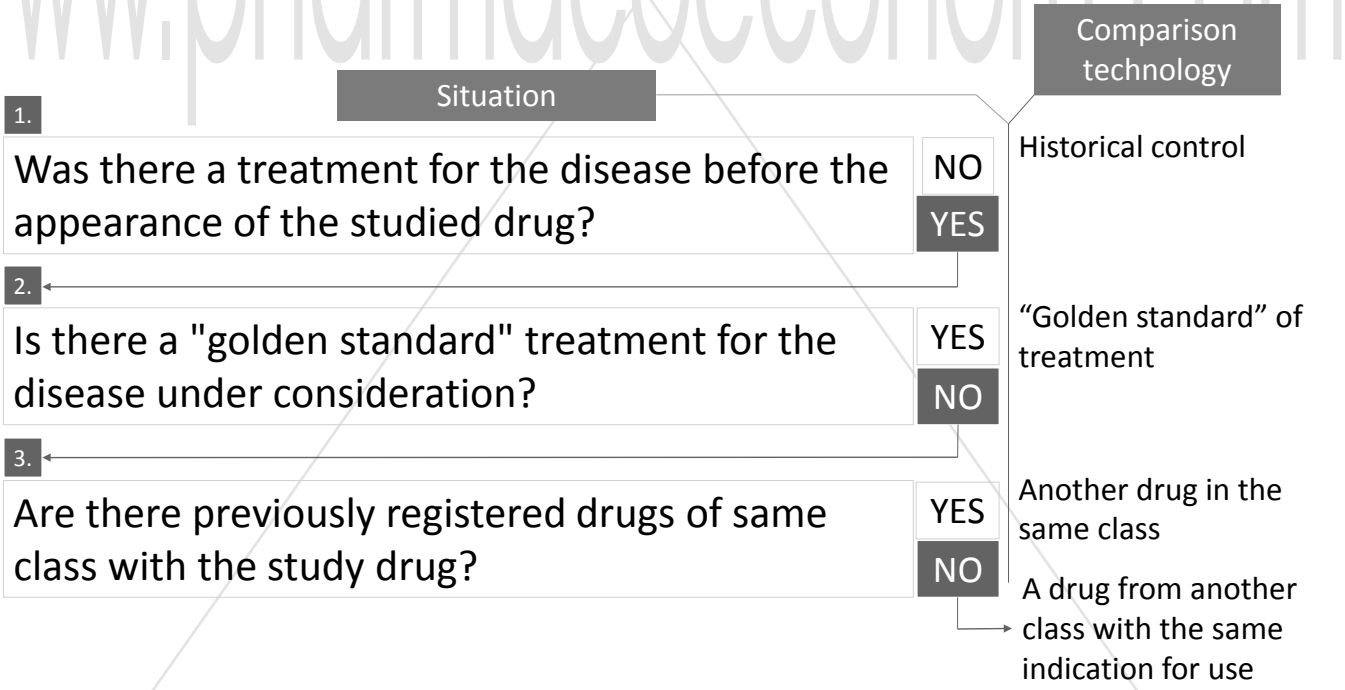


Figure 1. The algorithm for selecting comparison technologies in a pharmacoeconomic analysis with a traditional approach based on general indications for medical use

1 Provided that the criterion of effectiveness is LYG or QALY

Table 1. Baseline data and calculations for presented hypothetical situations

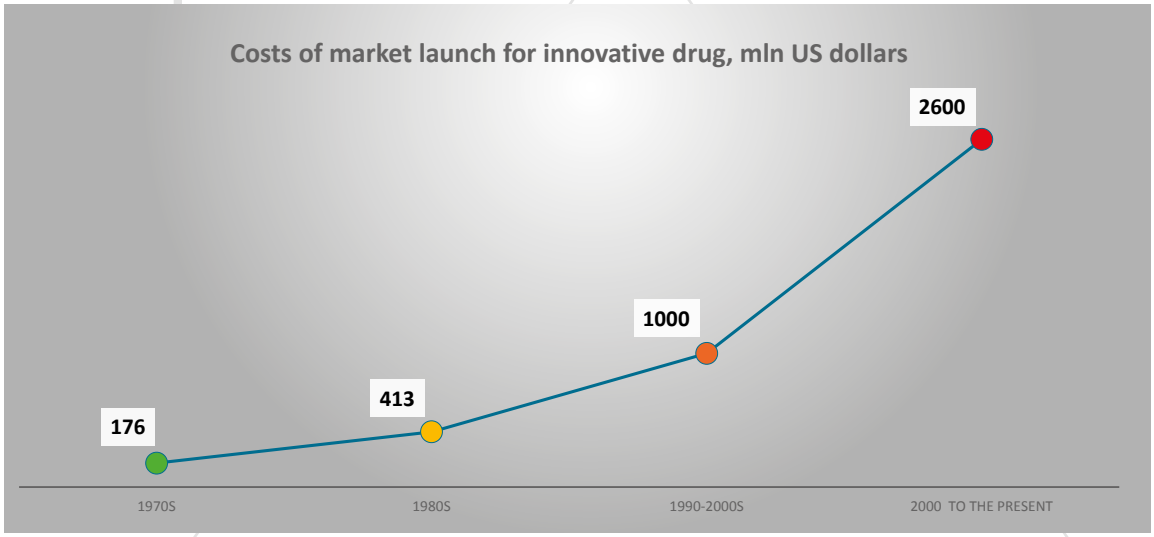
Technologies under consideration	Baseline data	A CER, RUB. For QALY	Comparison of CER drug X with CER of comparison technologies	ICER
An innovative X drug study for treating the M disease Cost per year for X: 2000 000 RUB.		2 531 646		
	Effectiveness of drug X: 0,79 QALY			
Hypothetical situation 1: Comparison with routinely outdated treatment (RT)	Cost per year for RT: 70000, RUB	700,000	2531646 > 700000 the hypothesis on the cost-efficiency of X	2797101 ICER exceeds the WTP of 1655757 rubles, X drug is unacceptable
	Effectiveness of drug X: 0,1 QALY			
Hypothetical situation 2: Comparison with other innovative drug (I)	Cost per year for I: 1.7 million, RUB	2 615 385	2531646 < 2615385 X drug as dominant	
	Efficiency of I: 0,65 QALY			

"Cost-efficiency" analysis results for a situation where comparison technology for X is routinely outdated treatment, show the unacceptability of innovative X because the CER value for it (2 531 646 RUB) is higher than for routine therapy (700 000 RUB), and the value ICER (2 797 101 RUB) exceeds the WTP (1 655 757 RUB). In the case of a different innovative drug in the role of comparison technology, the results of the "cost-efficiency" analysis show the advantage of the X - the CER's value for it (2 531 646 RUB) is less than for another innovative drug (2 615 385 RUB). According to the calculations, pharmacoeconomic conclusion for the same drug, depending on the comparison technique used, may be opposite. Thus, the selection of the comparison technology as a reference point in the coordinate system of the pharmacoeconomic analysis determines the result of the pharmacoeconomic evaluation.

At the same time, it is important to draw attention to the fact that the hypothetical situations under consideration are not artificially invented abstractions, but illustrate practical cases in pharmacoeconomic analysis. In fact, however effective the innovation in the pharmaceutical industry may be[2] efficiency gains cannot meet the rate of increase in costs especially if the comparison technology is a drug of 20-30 years old. In the example, the innovative drug X is nearly eight times more effective than routine therapy, but the cost of an innovative drug exceeds the cost of routine therapy more than 20 times! Figure 1 shows the evolution of the cost of developing an innovative drug over the past 40 years.

The timetable clearly shows a trend of a dramatic increase in the cost of developing innovative drugs, and also in accelerating the rate of increase in costs themselves. This fact, along with the transition from an era of blockbuster medicine (in which target groups of patients for drug number hundreds of thousands and even millions of people) to stratified and personalized medicine (which narrows the target groups of patients for innovative drugs to tens of thousands and hundreds of patients), result in a uncontrollable increase in the cost of innovative drug (Figure 2). Over the past few years, a symbol of high-value drugs was considered to be eculizumab (Soliris) (Fig. 3) [14], but according to data for September 2016, the most expensive drug in the world Is alipogene tiparvovec (Glybera), which is used to treat the lipoprotein lipase deficit, the cost of which is more than 50 000 USD. Taking into account the world-wide picture of the rate of additions in costs and effectiveness of drugs, that justifies the relevance of our hypothetical example, it is proposed to return to its further discussion.

The above example demonstrates that, in pharmacoeconomic assessment it is more favorable situation, when a comparison of the innovative drug is made with another (previously registered) innovative drug (This situation provides a more comparable level of costs, although the difference in efficiency between the two innovative drugs is also reduced). At the same time, if the assessable drug is a breakthrough drug in nosology that had no innovations for a long time, and the treatment has been carried out by outdated drugs, the use of outmoded routine as comparing technology reduces the likelihood of a positive pharmacoeconomic conclusion for the estimated innovative drug (though that innovative drug can provide a qualitatively different level of treatment outcomes, but the difference in costs between routine therapy



DiMasi JA, Grabowski HG, Hansen RW. Innovation in the pharmaceutical industry: new estimates of R&D costs. *J Health Economics*. 2016;47:20 33.

Congressional Budget Of ce (CBO). A CBO study: research and development in the pharmaceutical industry. www.cbo.gov/sites/default/ les/cbo les/ftpdocs/76xx/doc7615/10-02- drugr-d.pdf. Published October 2006. Accessed April 2016; Pharmaceutical Research and Manufacturers of America (PhRMA). PhRMA Annual Membership Survey, 1995-2015.Washington, DC: PhRMA; 2016

Figure 2. Evolution of the cost of developing innovative drugs.

2 A close attention to the situation of the pharmacoeconomic assessment of innovative drugs is due to the fact that in the vast majority of cases, new drugs(in the pharmaceutical market) and at high cost are the subject of pharmacoeconomic analysis.

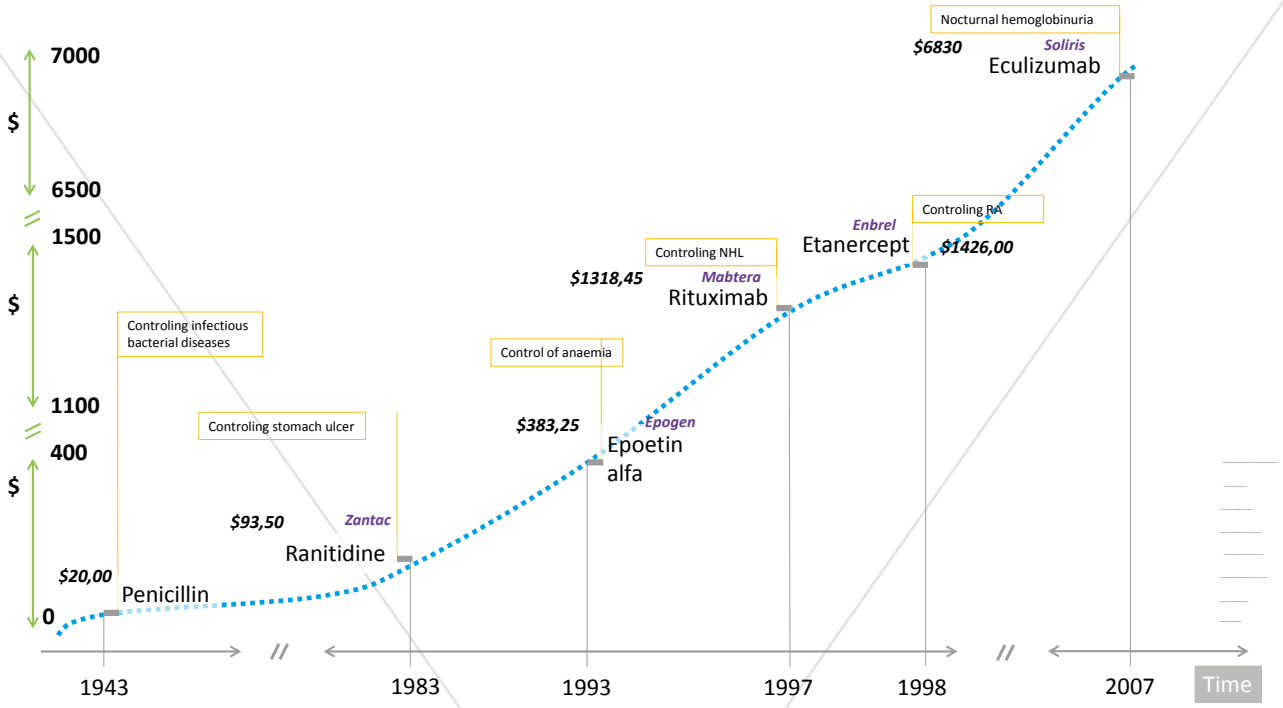


Figure 3. Evolution of the cost of innovative drugs packaging

and innovative drug is excessive. Obviously, the choice of technology has an even greater effect on the results of the "budget impact" analysis because it is expressed not as a unit but as an absolute monetary value that is directly dependent on the value of the cost.

In the present situation, it may appear that the interests of patients and doctors are ignored - in a disease that has already been endorsed by other innovative drugs in the recent past innovative drugs are more likely to obtain a positive pharmacoeconomic evaluation, which is a sine qua non for the inclusion of the medication in the drug programmes (reimbursable lists) as in Russia, and in most developed and developing countries in the world. However, there is a high risk of negative pharmacoeconomic conclusion in the introduction of innovative drugs in diseases in which innovation was previously absent, existing routine therapy is limited in efficiency and the need for modern efficient drugs is very high. This may question the adequacy of pharmacoeconomic analysis as a tool to support decision-making in the drug provision, if the pharmacoeconomic assessment makes it unlikely to introduce innovations into the most needy fields of medicine. However, in our view, with international experience, the existing problem is not related to the limited capacity of the pharmacoeconomic analysis methodology, but is a consequence of the incorrect use, which is the wrong point of reference, the comparison technology for the pharmacoeconomic assessment. The corresponding parallels can be made with using the maps in the navigation. They are used in long journeys between countries and cities and in short ones to find the location of an object (organization/theater/store/bank, etc.). However, in the case of a single object, the use of maps with a large scale (for example, maps of the whole territory of Russia) is inappropriate and unacceptable. Similarly, it will be an uncomfortable card with a small scale-up to the house numbers-when planning a long journey route. Likewise in the pharmacoeconomic analysis: the appropriate choice of comparison technology, as a reference point in the analysis coordinate system, will provide an adequate conclusion. On the other hand, the above facts suggest that a comparative pharmacoeconomic assessment of Contemporary Innovative drugs and drugs of routine practices, which were developed 20-30 years ago, often leads to inadequate conclusions.

However, this approach raises the problem of choosing another type of technology. This choice is transparent and evident if the reimbursed lists of drug programmes have previously included other relatively innovative drug with which an adequate comparative pharmacoeconomic assessment is possible. But what if the evaluated drug represents the first or only innovation in a specific therapeutic area, for which there was only outdated routine therapy previously?

In this situation, the solution may be to supplement the traditional principle of choosing the comparison technology based on the application of the evidence to the medical use of the level of innovation or the level of resource allocation (of course, subject to the comparability of clinical and socio-economic characteristics of therapeutic areas for which innovative drugs selected as comparison technologies are to be used in the pharmacoeconomic analysis). The proposed broadening of the approach to the choice of comparison technologies in the pharmacoeconomic analysis can be seen as a reflection of the central idea of pharmacoeconomics - optimizing the use of resources in the health system (from the price of treatment to the cost of the treatment result). It should be noted that in this case the key criterion determining the choice of the comparison technology is the characteristics of the innovation of the drug, depending on which appropriate comparison technology is chosen. This allows to specify the correct point of reference in the pharmacoeconomic study and, as a result, to obtain an adequate pharmacoeconomic assessment.

In the present situation, in which the pharmacoeconomic assessment is conducted for the first drug in the nosology class, which previously lacked products with a comparable level of innovation, efficiency and cost, the alternative approach we describe the choosing of the technology of comparison suggests comparing the "cost-efficiency" analysis with the "budget impact" analysis of drug with innovative products for other prescriptions. As a practical example of validity of the proposed approach to the selection of a comparison technology in the pharmacoeconomic analysis, we can use a foreign study adapted for Russia was made, the purpose of which was to evaluate the innovative drug in the direction of immunotherapy in the treatment of melanoma [15, 31]. In view of the lack of adequate comparison technology in the said medical prescription, the value of the unit of efficiency (1 month of life – LYM?), which was correlated with similar values for other innovative drugs already introduced in the treatment of various oncological diseases in Russia. In a coordinate system where the efficiency of the drugs (total monthly survival) was deferred, and on the abscissa axis, the cost of treatment for each of the drugs (Rub.) was determined on the basis of the efficiency and cost data, the points corresponding to the drug analysis were identified. In the next stage of the analysis, a trendline was built based on the values of the points indicated, reflecting the average cost of the unit of efficiency for the drugs in analysis, with a commensurate level of innovation and profitability. The specified trend line splits the plane of the graph into two semi-planes: the first semi-plane contained value of the unit value, which is less than the average cost per unit of efficiency. In contrast to the first semi-plane, the second included values that exceeded the average value of the unit of efficacy

of the drugs included in the analysis. From the pharmacoeconomics position, the results of the analysis are interpreted as follows: If the drug being studied falls into the first semi-plane, the using of health-care funds to the purchase of the drug can be regarded as a sound investment.

Thus, the example demonstrated the possibility of applying the proposed approach whereby comparison technology is chosen based not on the principle of conformity of the prescription to the medical use, but on the basis of the principle of the level of innovation and distribution of the resources in health system. The pharmacoeconomic analysis carried out in accordance with this approach has been characterized by an adequate selection of the point of assessment (scale), which has led to the necessary sensitivity of the analysis, increasing the likelihood of a relevant positive pharmacoeconomic conclusion and thus enhancing the availability of modern high-efficiency drugs for patients.

With the two approaches to the choice of comparison technology in the pharmacoeconomic analysis, there is a need to establish a rule governing the use of one or another approach. From our point of view, in accordance with the earlier reasoning, the key to applying each of approaches to the choice of comparison technology should be to establish an adequate level of sensitivity of the pharmacoeconomic analysis through the chosen comparison technology. Inequality (Formula 3) may be a reflection of compliance with the specified condition.

$$Cost(X) \leq Z \times Cost(A), \text{ where:} \qquad \text{Formula (3)}$$

Cost(X) – the total cost of the estimated innovative X drug per patient in the period under review, RUB;
Cost(A) – is the total cost of comparison technology (chosen on the basis of a general indications of medical use) per patient in the period under review, RUB;
Z – is the value that represents the number of times the cost of the drug studied exceeds the comparison technology (Z≥0).

To use a formula (3) condition, it is needed to define a value of Z. In practice, the value of Z can be empirically determined. The recommendation for a formalized setting of the Z parameter can be obtained and based on a scoring of the results of the pharmacoeconomic analysis in accordance with the decision of the governmental regulation of RF N871 of 28.08.2014. According to annex 6 of the regulatory act, the drug receives 10 points if its total cost is more than 80 per cent higher than that for the comparison technology. Then the equating Z with 10, according to the existing scoring system, will clearly reflect the incorrect comparison of innovative drug with the comparison technology chosen from the general statement approach to medical use. Thus, at Z≤2, the traditional approach based on a general statement of medical use should be used in the pharmacoeconomic study in selecting the comparison technology; At Z≥10 an alternative approach to the choice of comparison technology based on the comparability of the drug level of innovation should be used. Based on the discourses presented, the general algorithm for selecting the comparison technologies in the pharmacoeconomic analysis appears in the following form (Figure 5). According to this algorithm, the first step in choosing a comparison technology is to use the principle of general indication for medical use, then the selected comparison technology and the evaluated drugs are tested against the Z criteria, and results allow to use the selected comparison technology or to choose other comparison technology, but on the basis of an alternative principle of comparability between the levels of innovation of the drug in pharmacoeconomic analysis. This sequence of actions in the selection of the comparison technology in the context of the pharmacoeconomic research ***for innovative*** drugs ensures that the sensitivity of pharmacoeconomic analysis is adequately set and considered conclusions are received.

Bibliography:

1. Kulikov A.Yu., Ugrekhelidze D.T., Larionova V.B., Snegovoy A.V. Pharmacoeconomic analysis of granulocyte colony-stimulating factors in the prevention of febrile neutropenia of cancer patients under health conditions of the Russian Federation//Pharmacoeconomics: theory and practice. -2016. -Vol. 4, №1. P.188-194.
2. Kulikov A.Yu., Babiy V.V., Shestakova I.V. Pharmacoeconomic analysis of the use of a combination of daclatasvir and asunaprevir drugs for the treatment of chronic hepatitis C in the territory of the Russian Federation// Pharmacoeconomics: Theory and practice. 2016. -Vol. 4, No.1. -P. 123-130
3. Kulikov A.Yu., Skrypnyk A.R. pharmacoeconomic analysis of the monofer drug (iron III-hydroxide olygoisomaltosate) in the treatment of iron deficiency anaemia//Pharmacoeconomics: theory and practice. -2016. -Vol. 4, №1. P.183-186.
4. Kulikov A.Yu., Petrovsky A.V., Rybchenko Yu.V., Skrypnyk A.R. Pharmacoeconomic analysis of the use of the drug lapatinib in treating breast cancer with HER2 + tumourous expression//Pharmacoeconomics: theory and practice. -2016. -Vol. 4, №1. P.53-60.
5. Ugrekhelidze D.T, Kulikov A.Yu. pharmacoeconomic analysis of the drug Velphoro ® 500 (β-iron (III) oxyhydroxide, sucrose and starch) in the treatment of hyperphosphataemia patients with chronic kidney disease// Pharmacoeconomics: theory and practice. -2016. -Vol. 4, №1. P.176-182.
6. Arinina E.E., Kulikov A.Yu., Tolordava G.A. Comparative pharmacoeconomic analysis of medication for acute decompensation of heart failure in Russia//Pharmacoeconomics: theory and practice. 2016. -T. 4, No. 1. -C. 169-175
7. Abdrashitova G.T., Kulikov A.Yu. Pharmacoeconomic analysis of the use of haemin medication in treating patients with acute intermittent porphyria in the Russian Federation//Pharmacoeconomics: Theory and practice. 2016. -Vol. 4, No.1. -P. 165-168
8. Kulikov A.Yu., Pochuprina A.A. Pharmacoeconomic assessment of the use of abatacept for rheumatoid arthritis patients with insufficient response to methotrexate therapy in the Russian Federation//Pharmacoeconomics: Theory and practice. 2016. -Vol. 4, No.1. -P. 116-122
9. Novikov I.V., Kulikov A.Yu. Pharmacoeconomic analysis of the use of metformin extended release in Diabetes mellitus 2 type//Pharmacoeconomics: Theory and practice. 2016. -Vol. 4, No.1. -P. 88-94
10. Tolordava G.A., Arinina E.E., Kulikov A.Yu. Pharmacoeconomic analysis

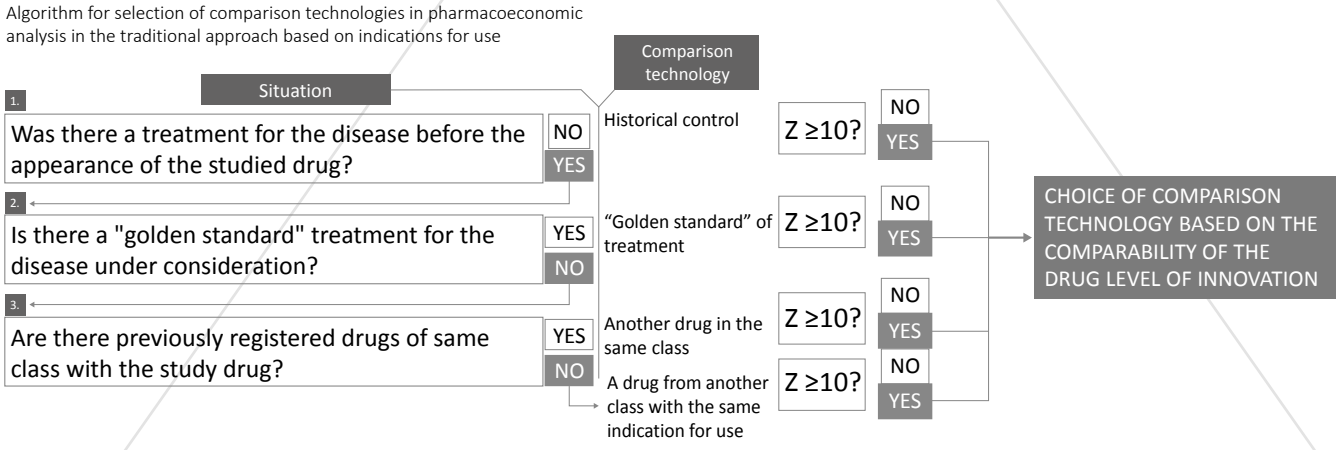


Figure 5. The algorithm for selecting the comparison technology in the pharmacoeconomic assessment of innovative drug

of Fozinopril drug in the treatment of patients with arterial hypertension// Pharmacoeconomics: theory and practice. -2015. -Vol. 4, №1. P.70-78.
11. Kolbin A.S., Kurylev A.A., Pavlysh A.V., Pavlysh A.V., Balykin Yu.E. Pharmacoeconomic analysis of drugs used in the first line of targeted therapy metastatic kidney cancer//Pharmacoeconomics: Theory and practice. 2014. -Vol. 2, .№3. -P. 14-20
12. Kulikov A. Yu, Babiy V.V. Pharmacoeconomic analysis of the use of Eviplera (rilpivirine /tenofovir/emtricitabine) for the treatment of HIV-positive patients on the territory of the Russian Federation//Pharmacoeconomics: theory and practice. -2015. -Vol. 3, №1. P.35-43.
13. Yagudina R.I., Kulikov A.Yu., Serpik V.G. Pharmacoeconomics: Teaching aid-Rostov-on-Don: Phoenix, 2017. -237 P.
14. Pharmvestnik. [Electronic resource] -Access Mode: https://www.pharmvestnik.ru/publs/lenta/v-mire/18124.html#.WVbHscZeNPM
15. Kulikov A.Y., Skrypnyk A.R. Analysis of the relative value of the use of ipilimumab medication in patients with metastatic melanoma//Pharmacoeconomics: Theory and practice. 2016. -Vol. 4, No.4. -P. 121-127
16. Kolbin A.S., Kurylev A.A., Vilyum I.A., Proskurin M.A., Balykina Yu.E. Pharmacoeconomic analysis of the use of vemurafenib to treat inoperable or metastatic melanoma in patients with the mutation of BRAF V600//Pharmacoeconomics: theory and practice. -2015. -Vol. 3, №4. P.-15-20.
17. Kolbin A.S., Vilyum I.A., Proskurin M.A., Balykina Yu.E. Pharmacoeconomic analysis of the use of Telavancin in therapy for patients with complicated skin and soft tissue infections in the health conditions of RF//Pharmacoeconomics: Theory and practice. 2016. -Vol. 4, No.2. -P. 75-81
18. Cost-Effectiveness Analysis of Tyrosine Kinase inhibitors to Patients with Advanced gastrointestinal stromal tumors. Nerich V, Fleck C, Chaigneau L, Isambert N, Borg C, Kalbacher E, Jary M, Simon P, Pivot X, Blay JY, Limat S. Clin Drug Investig. 2016 Sep 24.
19. Cost-effectiveness of bortezomib for multiple myeloma: a systematic review. Chen W, Yang Y, Chen Y, Du F, Zhan H. Clinicoecon Outcomes Res. 2016 May 3;8:137-51.
20. Cost-effectiveness of first-line erlotinib in patients with advanced non-small-cell lung cancer unsuitable for chemotherapy. Khan I, Morris S, Hackshaw A, Lee SM. BMJ Open. 2015 Jul 2;5(7):e006733.
21. Cost-effectiveness of obinutuzumab for chronic lymphocytic leukaemia in The Netherlands. Blommestein HM, de Groot S, Aarts MJ, Vemer P, de Vries R, van Abeelen AF, Posthuma EF, Uyl-de Groot CA. Leuk Res. 2016 Sep 3;50:37-45.
22. Cost-effectiveness of treatment strategies for BRAF-mutated metastatic melanoma. Curl P, Vujic I, van 't Veer LJ, Ortiz-Urda S, Kahn JG. PLoS One. 2014 Sep 8;9(9):e107255.
23. An economic evaluation of docetaxel and paclitaxel regimens in metastatic breast cancer in the UK. Benedict A, Cameron DA, Corson H, Jones SE. Pharmacoeconomics. 2009;27(10):847-59.
24. The use of irinotecan, oxaliplatin and raltitrexed for the treatment of advanced colorectal cancer: systematic review and economic evaluation. Hind D, Tappenden P, Tumur I, Eggington S, Sutcliffe P, Ryan A. Health Technol Assess. 2008 May;12(15):iii-ix, xi-162.
25. Cost effectiveness of pegaptanib for the treatment of age-related macular degeneration in the UK. Wolowacz SE, Roskell N, Kelly S, Maciver FM, Brand CS. Pharmacoeconomics. 2007;25(10):863-79.
26. Cost-effectiveness of ceritinib in patients previously treated with crizotinib in anaplastic lymphoma kinase positive (ALK+) non-small cell lung cancer in Canada. Hurry M, Zhou ZY, Zhang J, Zhang C, Fan L, Rebeira M, Xie J. J Med Econ. 2016 Oct;19(10):936-44.
27. Cost-Effectiveness Analysis of Different Sequences of the Use of Epidermal Growth Factor Receptor Inhibitors for Wild-Type KRAS Unresectable Metastatic Colorectal Cancer. Riesco-Mart nez MC, Berry SR, Ko YJ, Mittmann N, Giotis A, Lien K, Wong WW, Chan KK. J Oncol Pract. 2016 Jun;12(6):e710-23.
28. Erlotinib and gefitinib for treating non-small cell lung cancer that has progressed following prior chemotherapy (review of NICE technology appraisals 162 and 175): a systematic review and economic evaluation. Greenhalgh J, Bagust A, Boland A, Dwan K, Beale S, Hockenhull J, Proudlove C, Dundar Y, Richardson M, Dickson R, Mullard A, Marshall E. Health Technol Assess. 2015 Jun;19(47):1-134.
29. Sipuleucel-T for the Treatment of Metastatic Hormone-Relapsed Prostate Cancer: A NICE Single Technology Appraisal; An Evidence Review Group Perspective. Simpson EL, Davis S, Thokala P, Breeze PR, Bryden P, Wong R. Pharmacoeconomics. 2015 Nov.; 33 (11): 1187-94.
30. Cost-effectiveness analysis alongside clinical trials II is a Ispor good Research practices Task Force report. Scott D. Ramsey, MD, Ph.D., Richard J. Willke, Ph.D., Henry Glick, Ph.D., Shelby D. Reed, Ph.D., RPh, Federico Augustovski, MD, MSc, Phd6, Bengt Jonsson, Ph.D., Andrew Briggs, MSc, DPhil, Sean D. Sullivan, PhD. Value in Health 18 (2015) 161-172
31. The Relative Clinical and the Economic Value of ipilimumab in the Treatment of Metastatic Melanoma, Versus Other, Anti-Cancer agents for Metastatic, from a Diseases to the Private Health care System perspective. Stefani S, Tanaka S, Araujo R, piece K, Bernardino G, Donato BM. Value Health. 2015 Nov.; 18 (7): a819. Doi: 10.1016/J. Jval 2015.09.250. Epub 2015 OCT 20.