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PHARMACOECONOMIC STUDY OF BUSERELIN-DEPO IN THE TREATMENT OF HORMONE-DEPENDENT PROSTATE CANCER

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Abstract: *Pharmacoeconomic study comparing luteinizing hormone-releasing hormone agonists (LHRH-A), used for prostate cancer treatment was conducted. The study included drugs: buserelin, goserelin, triptorelin and leuprorelin. Pharmacoeconomic study included the following methods: cost analysis, cost-effectiveness analysis, cost minimization analysis and budget impact analysis. The time horizon for cost analysis, cost minimization analysis and budget impact analysis amounted to 1 year, whereas for cost-effectiveness analysis it was equal to 6 months. Direct costs were taken into account. As a result, it was found that annual costs for the treatment of one patient for each of the considered drugs (buserelin, goserelin, triptorelin and leuprorelin) respectively accounted for 55 169 rubles, 90 130 rubles, 90 133 rubles и 94 599 rubles. Results of the budget impact analysis showed that the annual budget per patient using drug therapy buserelin, goserelin, triptorelin and leuprorelin respectively amounted to 129 545 rubles, 164 506 rubles, 164 509 rubles and 168 974 rubles. Cost minimization analysis demonstrated that under the assumption of equal clinical effectiveness review of medications, annual treatment of one patient using buserelin is characterized with 34 961 rubles compared with goserelin and 39 430 rubles compared with leuprorelin. Cost-effectiveness analysis using the criterion of decreasing the prostate-specific antigen (PSA) level, it was found that buserelin is characterized with the greatest rate of decrease in the PSA value, so it has the smallest value of the cost-effectiveness ratio and, thus, relative to the comparison drugs is strictly preferred drug.*

Key words: *pharmacoeconomic study, cost-effectiveness analysis, cost minimization analysis and budget impact analysis, hormone-dependent prostate cancer, buserelin, goserelin, leuprorelin, triptorelin.*

In recent years, the use of domestically manufactured drugs is becoming prioritized policy in the field of drug supply in the Russian Federation. In this regard, the use of the medicinal product of the domestic production buserelin (Buserelin-Depo, CJSC «Pharm-Sintez») luteinizing hormone-releasing hormone agonist (LHRH-A) intended for drug therapy of hormone-dependent prostate cancer in the state program of drug supply is relevant. Currently, the drug Buserelin-Depo is not included in the list of essential medicinal products and therefore cannot be used in state programs of drug supply. For this reason, there is a need for the inclusion of this drug in the of medicinal products for medical application lists, according to the current rules of formation of lists of drugs for medical application, approved by Government Decree of RF dated 30.08.2014 N871 [1], therefore it is required to perform a pharmacoeconomic evaluation of the drug. Conducted Information retrieval revealed one domestic pharmacoeconomic study dating 2010 and comparing the use of LHRH-A in prostate cancer therapy [2]. In their study, Apolikhin O. I. and colleagues [2] used the Buserelin-Depo drug as a comparison drug. However, a detailed analysis of this publication showed that the pharmacoeconomic calculations are irrelevant now. This study used the price of the drug Buserelin-Depo 8 217,58 rubles per unit dosage 3.75 mg, whereas in the present time the price of the product is 4 200 rubles., that is lower than the price used in pharmacoeconomic calculations by Apolikhin O. I. and colleagues at 51%. In addition, the results of pharmacoeconomic studies are also restricted by using the rate of introduction of injection LHRH-A, which amounted 3 900 rubles per visit (injection) [2]. Based on the foregoing, a new pharmacoeconomic evaluation of drug Buserelin-Depo was performed that met current health care system conditions, for a proposal for its inclusion in the lists of medicines for medical application.

The purpose of the described pharmacoeconomic study was to identify from the perspective of pharmacoeconomic parameters the most preferred drug of the group of LHRH-A for the treatment of hormone-dependent prostate cancer.

In the pharmacoeconomic study, the researchers analyzed LHRH-A drugs included in the standard of specialized medical care of malignant tumors of the prostate in particular drugs: buserelin, goserelin, leuprorelin and triptorelin (table 1) [7,8,9].

Table 1. Drugs and their corresponding drugs included in pharmacoeconomic analysis

International non-propriety name	Brand name	Manufacturer
Buserelin	Buserelin Depo	CJSC "Pharm-Sintez" - Russia
Goserelin	Zoladex	AstraZeneca UK Limited – United Kingdom; Manufacturer of primary package - AstraZeneca UK Limited; Manufacturer of secondary package, Manufacturing control.-CJSC "ZiO-Zdorovie" - Russia.
Triptorelin	Diphereline	"Ipsen Pharma" - France; Manufacturer of primary package, Manufacturer of secondary package, Manufacturing control – Ipsen Pharma Biotech - France.
Leuprorelin	Lucrin Depot	Owner- Abbott Laboratories S.A., Spain; Manufacturer- Takeda Pharmaceutical Company Limited, Japan; Manufacturer of primary and secondary package, Manufacturing control- Abbott Laboratories S.A., Spain.

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In the described study, the following methods of pharmacoeconomic analysis were used: cost analysis, cost-effectiveness analysis, cost minimization analysis and budget impact analysis. The time horizon for cost analysis, cost minimization analysis and budget impact analysis amounted to 1 year, whereas for cost-effectiveness analysis it was equal to 6 months. Direct costs were taken into account, as well as the cost of medical services for the treatment of prostate cancer according to the tariffs of MFOMS (Moscow Fund of obligatory medical insurance) [10]. Thus, a pharmacoeconomic study of goserelin, triptorelin and leuprorelin included analysis of registered maximum prices without VAT (because they are included in the essential drugs list). For drug buserelin – Buserelin Depo a registered maximum price was absent, therefore in this connection has been used the recommended price of the manufacturer CJSC «Pharm-Sintez» (table 2).

Table 2. Prices for drugs included in study

Brand name	Dosage form	Price of pack, rubles
Buserelin Depo	Lyophilisate for suspension for intramuscular injection prolonged action, 3.75 mg (vial) 320.93 mg x 1 + solvent (vial) 2 ml x 1 + (syringe) x 1 + (needle) x 2 + (alcohol swab) x 2	4 200,00 ₽
Zoladex	Capsule for subcutaneous injection, prolonged action, 3.6 mg - syringe-applicator with protective mechanism (system safety introduction Safety Glide) (1) - cardboard pack	6 880,10 ₽
Diphereline	Lyophilisate for suspension for intramuscular injection prolonged action 3.75 mg - vials /kit with solvent: 0.8% mannitol solution (ampoules) 2 ml, disposable syringe and needle for injection-2/ pack –cardboard packs	6 880,32 ₽
Lucrin Depot	Lyophilisate for suspension for intramuscular and subcutaneous injection, prolonged action, 3.75 mg, set: ((two-chamber syringes) 44.1 mg of lyophilized powder and 1 ml solvent /complete with plastic piston, single needle for injection and one or two wipes//) N1	7 222,66 ₽

At the first stage of pharmacoeconomic research, cost analysis was carried out [4]. In the beginning, the annual cost of one patient therapy with each drug was determined, which was calculated based on the above prices for drugs and dosage of drugs. In accordance with the instructions for use of all study drugs were administered 1 time per 4 weeks at a dosage of 3.6 mg goserelin (p/injection), and 3,75 mg for buserelin, triptorelin and leuprorelin (I. m. injection) [7]. In addition, during calculating the annual cost of pharmacotherapy RPG were taken into account the cost of their introduction: the value of the p/to the injections, and in/m injection, according to the tariffs of MPAS was 29,27 rubles [10]. Based on the above data, the annual costs per patient amounted to drug Buserelin Depot, Zoladex, Diphereline and Lucrin Depot 55 169,32 rubles, 90 130,26 rubles, 90 133,13 rubles and 94 598,84 rubles respectively (figure 1).

As follows from the data presented in figure 1, the drug Buserelin Depo was characterized by the lowest value of the annual cost of therapy.

In the next phase of pharmacoeconomic research budget impact analysis was performed. [4]. In the analysis process the total annual cost of patients with prostate cancer therapy with each drugs was calculated, which included the amount of the annual cost of treatment with each of the studied drugs and the cost of medical services in the treatment of prostate cancer, which is in accordance with the tariffs of MFOMS was 74 375,44 rubles. The results of the analysis of budget impact analysis showed that the budget per patient during drug therapy with Buserelin Depo, Zoladex, Diphereline and Lucrin Depot respectively amounted to 129 544,76 rubles, 164 505,70 rubles, 164 508,57 rubles and 168 974,28 rubles. Thus, the drug Buserelin Depo has the lowest budget for the treatment of prostate cancer from the considered alternatives.

During pharmacoeconomic research the efficiency analysis was carried out by means of information retrieval [6]. The only national study that directly compared the efficacy of with studied medications was found. Study by Mishugin S. V. and colleagues, 2014 evaluated the efficacy and safety of buserelin therapy in patients with locally advanced and metastatic hormone-dependent prostate cancer, in comparison with other drugs of the LHRH-A group– goserelin, triptorelin and leuprorelin. The study by Mishugin S. V. and colleagues, 2014 [3] involved 86 patients who were divided into two groups – one receiving buserelin and second - receiving other LHRH-A group drugs. It was found that the PSA level in the group of patients treated with buserelin, have declined over the 6 months from 105.2 ng/ml at entry to the study to 3.2 ng/ml at the end of the study, while in the group of patients who were taking alternative medications had a decline in PSA level from 94,7 ng/ml to 3.01 ng/ml. However, it should be noted that this work has not been provided with the results of statistical processing of the obtained data, as a consequence, there is no confidence in the presence of a statistical difference in PSA between the compared treatment groups. In this regard, two scenarios were described in pharmacoeconomic study. The first assumed no difference in effectiveness between the drugs, which is a criterion of application of cost-minimization method [4]. The second scenario was based on the assumption that the difference in PSA levels between the compared groups of patients in a clinical study by Mishugin S. V. and colleagues, 2014 statistically significant, which required cost-effectiveness analysis [5].

Cost-minimization analysis [4] was based on previously obtained results of the budget impact analysis and allowed to answer the question of how costs will change when transferring patients using goserelin, triptorelin and leuprorelin on buserelin. The results of the cost minimization analysis showed that the patients transfer from Zoladex, Diphereline and Lucrin Depot on Buserelin Depo accompanied by savings of 34 961 rubles, 34 964 rubles and 39 430 rubles respectively (figure 2).

At the final stage of pharmacoeconomic studies a second scenario for efficiency analysis was calculated, according to which the efficiency between the buserelin and other LHRH-A drugs has statistically significant differences. In this case, cost-effectiveness analysis was used [5], which allows to determine the cost of achieving a unit of effectiveness for each of the treatment regimens. The criterion of effectiveness was the reduction of PSA level on each of treatment regimens. As used in study by Mishugin S. V. and colleagues, 2014 there was not detailed information about the specific values of the patients distribution using drugs goserelin, triptorelin and leuprorelin, given their close cost us, the assumption was made that the patients were distributed between these drugs in equal shares (33.3% of patients received goserelin, triptorelin and leuprorelin). The time horizon of the cost-effectiveness analysis was similar to the one in a clinical study and equaled 6 months. For drug Buserelin Depo cost-effectiveness ratio means is a cost of PSA decrease per unit amounted to 249 rubles, and for therapies involving drugs goserelin, triptorelin and leuprorelin – 460 RUB. (figure 3).

As follows from the data presented in figure 3, buserelin was characterized by the lowest value of the cost-effectiveness ratio, and from cost-effectiveness perspective, it was considered strictly preferred drug. The results of cost minimization analysis and cost-effectiveness analysis were checked with the single-factor sensitivity analysis increasing the cost of Buserelin Depo at 25%.

Conclusion

Conducted pharmacoeconomic study of luteinizing hormone-releasing hormone agonists used for prostate cancer treatment revealed the advantage of buserelin (Buserelin Depo) from the position of cost minimization analysis, budget impact analysis and cost-effectiveness analysis, which suggests the dominance of Buserelin Depo under considered among luteinizing hormone-releasing hormone agonists.

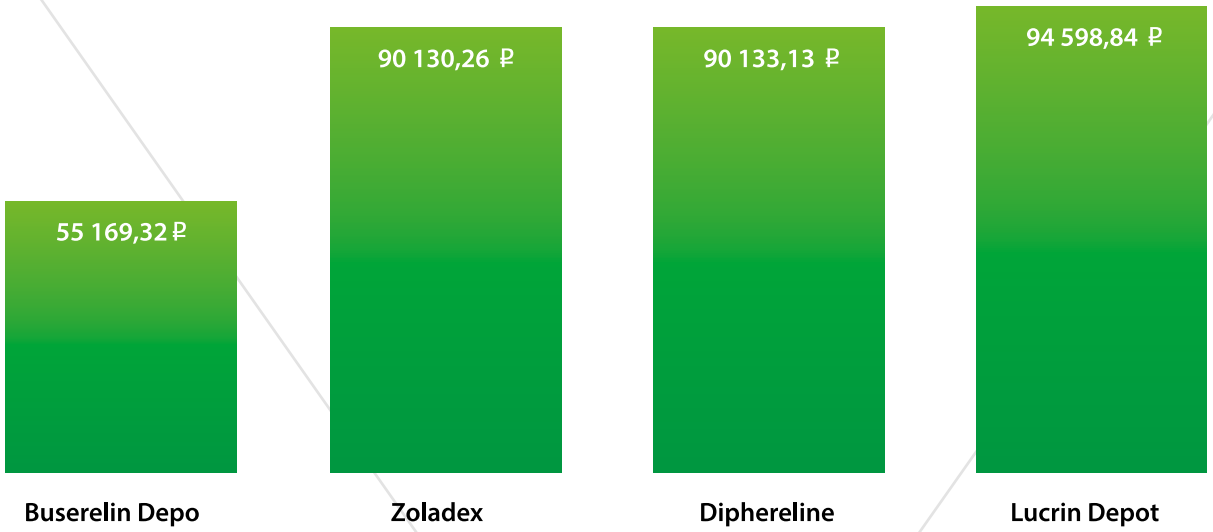

Figure 1. The results of the costs of analyzed drugs per patient in one year.

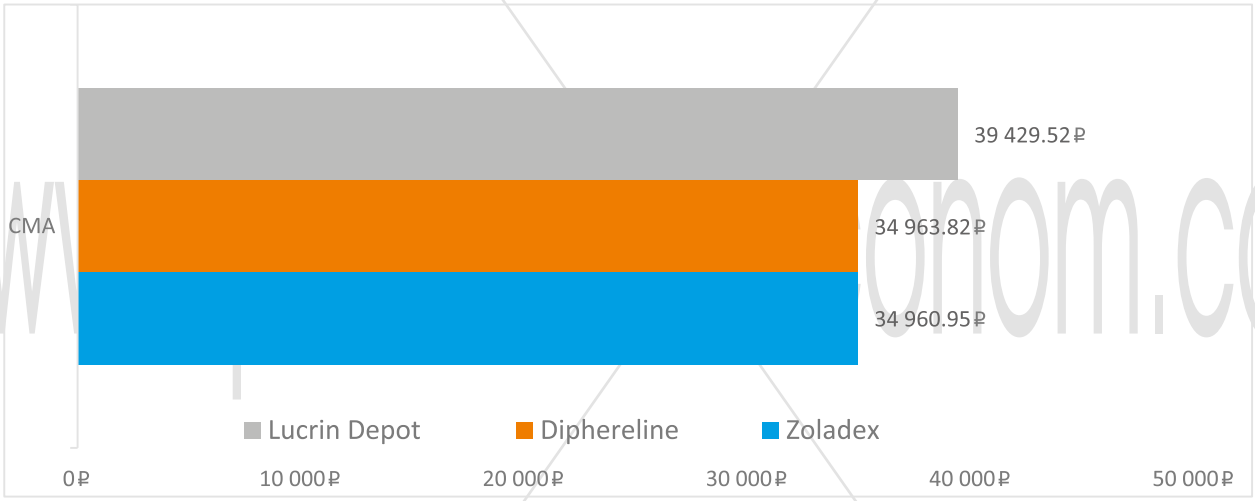

Figure 2. The results of cost minimization analysis - money saving during transfer of patient using drugs Zoladex, Diphereline or Lucrin Depot on Buserelin Depo.

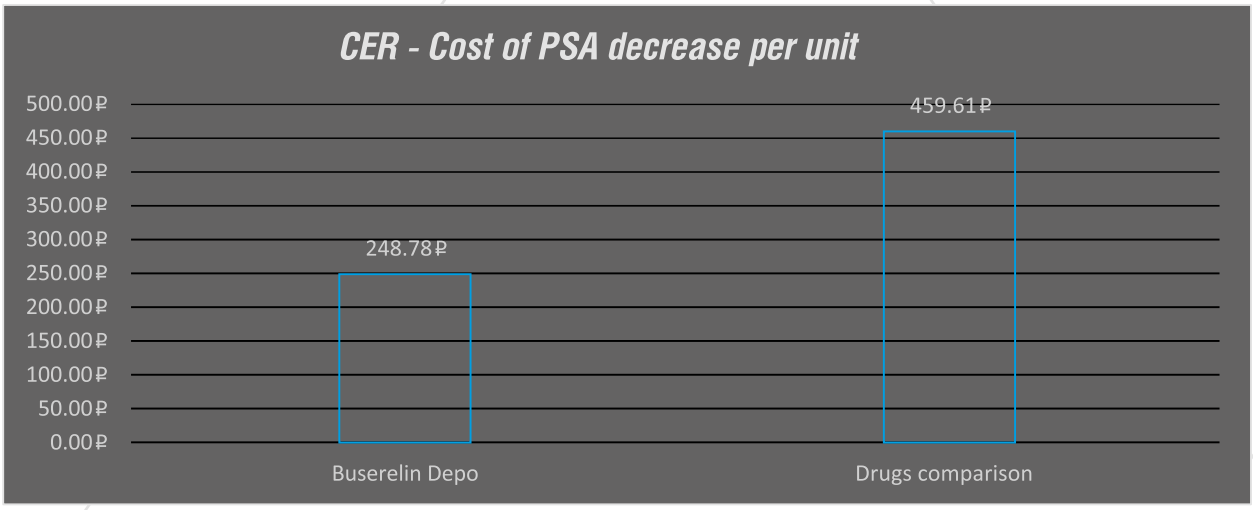

Figure 3. The results of the cost-effectiveness analysis

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