

APPROACHES TO RESEARCHING REFERENCE PRICES FOR INSULIN DRUGS

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Abstract

Diabetes mellitus is a serious incurable disease that requires special from society and the government due to its high prevalence, severity of complications and the high cost of treatment, diagnosis and self-monitoring. Therefore, the development of an effective system of price regulation and cost recovery to ensure maximum coverage is an actual problem of modernity. The study of the state of pharmaceutical supply of patients with type I diabetes in 2015-2021 allowed us to identify the main trends – changes in the structure and dynamics of insulin consumption in the hospital and retail (pharmacy) segment in connection with the introduction and implementation of a pilot project to reimburse their cost. It has been established that most domestically produced drugs have prices lower by 2.5-14% than the average in reference countries.

Moreover, in many countries (Hungary, Romania, Slovakia, Greece, Poland, the Czech Republic), insulin prices are lower than those declared in Ukraine. This must be taken into account when choosing reference countries. The analysis shows that in most European countries, external analysis analyses the indicators of wholesale prices in more than 10 countries. Based on the results of a comprehensive study, a generalized model of reference pricing has been developed, which is substantiated by calculations and is optimal for modern conditions.

Keywords: *drug availability, reference pricing, insulin preparations*

Introduction

Diabetes mellitus (DM) as one of the most important global medical and social problems, due to the wide spread of the disease, the severity of complications, the high cost of diagnostic and treatment tools. Despite significant advances in diabetology, diabetes remains incurable, and to maintain life and ability to work, the patient must constantly receive insulin replacement therapy.

Recognizing the threat that diabetes poses to humanity, the UN General Assembly adopted a Resolution on Diabetes on December 20, 2006 and called for a concerted effort to combat diabetes. Expenditures related to the provision of medical care to patients are estimated at 2-3% of total health care expenditures; almost 80% account for the treatment of complications, 20% - for the purchase of antidiabetic drugs and controls [4]. According to IDF, the cost of treatment of one patient with at least one chronic complication is on average from 6 to 18 thousand dollars. USA per year [1].

In line with the global goals of the WHO and the UN, it is envisaged to achieve general medical coverage for the population by 2030 and a 30% reduction in premature deaths from non-communicable diseases, including diabetes. However, many countries currently do not have a national diabetes treatment plan, and about 50% of the world's population does not have full coverage of basic health services.

At the present stage of reforming the domestic health care system and the public procurement system, the mechanisms of reference pricing and reimbursement of medicines (drugs) for the treatment of severe chronic diseases, in particular, type I and II diabetes, are being tested.

Thus, reference pricing in Ukraine has been introduced since 2012 in connection with the implementation of a pilot project on state regulation of prices for antihypertensive drugs. In the process of developing the regulatory framework for state regulation of prices for insulin drugs, since 2014, approaches to the formation of reference prices have repeatedly changed due to a number of both objective and subjective factors. However, in our opinion, the current approaches to pricing and reimbursement of insulin drugs need to be improved in terms of methodology, in particular,

justification of the choice of reference countries and the actual methodology for determining reference prices taking into account both world experience and national health system. At the same time, the problem of improving the effectiveness of providing patients with diabetes with available insulin drugs remains unresolved.

Methods

The object of the study were scientific publications, statistics, price indicators, official websites of the authorized bodies of reference countries. The research was conducted using methods of analysis, systematization and generalization, mathematical and statistical calculations.

Results

At the first stage, an analysis of epidemiological indicators - the incidence and prevalence of diabetes in Ukraine and the world. It has been established that since 2000, the prevalence of diabetes (type I and II, diagnosed and undiagnosed) among people aged 20-79 has more than tripled - from 151 million (at that time 4.6% of the world's population) to 463 million (respectively 9.3%). According to experts, in 2030 the number of patients with diabetes will increase to 578 million (10.2% of the population), in 2045 - to 700 million (10.9%).

According to the WHO, the European region ranks third in the number of diabetics in the world (60 million) - this is 1 in 11 adults, with more than a third (41%) of people with diabetes without a diagnosis, so there is a high risk development of complications. 31% of deaths related to diabetes are in people under the age of 60. Also in Europe, most children and adolescents suffer from type I diabetes (296.5 thousand). According to the International Diabetes Federation IDF, in Europe the first places in the number of diabetics in 2019 are occupied by Germany - 9.5 million, Russia - 8.3 million, Turkey - 6.6 million, Italy - 3.7. million, Spain - 3.6 million

The annual global cost of treating diabetes is estimated at \$ 760 billion. and is projected to reach \$ 825 billion by 2030. USA. Europe's \$ 161 billion in diabetes costs USA, ie 21% of total world spending [1]. Insulin access and availability are influenced by political and socio-economic factors at both the global and national levels. At the same time, one of the main factors is unreasonable margins in the supply chain of drugs. Sales prices for drugs range

from 2.24 to 43.51 dollars. US (median - \$ 5.99) for human insulin and from 6.88 to 81.67 dollars. (median - \$ 34.20) for analog insulin per 10 ml, 100 international units (IU) equivalent in a vial [1]. It should be noted that in most countries, patients receive insulin free of charge, less often - on a co-payment basis. With regard to analogues, in many Central and Eastern European countries, payers recognize the benefits of analogue insulins, but insist on limiting their use due to the excessive cost and limited resources of health [5]. In the public sector, the average price of human insulin is \$ 7.64 US dollars (from 2.16 to 36.70 US dollars), by analogy - 6 times higher. In the private sector, human insulin and analogues cost 3 and 5 times higher than the vial equivalent of 10 ml, 100 IU. According to experts, based on cost indicators, the annual cost of human insulin preparations of medium duration should be \$ 72. US dollars, and for long-acting analogues - 133 dollars. US, which is an order of magnitude lower than actual costs [1].

Key elements of the model of reference pricing for insulin drugs that need improvement. are as follows:

- 1) determination of criteria for the distribution of insulin drugs into reference groups (RG);
- 2) reference countries (justification of choice);
- 3) the method of calculating the wholesale and reference price.

The methodology of reference pricing involves the formation of reference groups, therefore, according to the ATX classification, we have divided insulin preparations into 4 groups according to the speed and duration of action.

We conducted an analysis of the domestic insulin market. Insulin drugs are biotherapeutic drugs (BP), which are divided into reference and similar. Today, there are more than 200 insulin preparations and analogues in the world, which differ in clinical and pharmacological characteristics, duration of action, degree of purification and allow the use of different modes of insulin therapy (2-4 or more injections per day).

As of October 1, 2021. 193 trade names are registered in the State Register of Medicinal Products, of which 171 are finished medicinal products, 6 are powders (substances) for pharmaceutical use and 16 are in bulk dosage forms. Among the registered drugs, only 13.47% are

domestic (26 items), 9.85% are co-produced (19 drugs) and 76.68% are foreign (148 drugs) [7].

It is established that the Ukrainian market is dominated by drugs manufactured by the world's leading pharmaceutical companies Novo Nordisk (Denmark), Sanofi-Aventis (Germany), Lilly France (France), Bioton (Poland). Domestic manufacturers (PJSC "Farmak", PJSC "For the production of insulin" Indar ") are focused on the production of Insulin human groups A10AB01, A10AD01, A10AC01 mainly in the form of vials (5 ml and 10 ml) and cartridges. Pre-filled syringe pens are produced only by foreign companies [8].

In the register of reference prices (refund prices) for insulin drugs as of 1.10.2021 (order of the Ministry of Health of 17.03.2020 № 668) officially set prices for 77 trade items (of which 45 - imported drugs (which is 58.4%), 21 - domestic production (27.3%), 11 - joint production with the participation of German or Indian companies (14.3%)) [9].

It should be noted that in Ukraine from 2019 the drug A10AE54 Insulin glargine and lixisenatide Solikva (Sanofi-Aventis, Germany) is subject to reimbursement. Soliqua is used to treat type II diabetes and is non-refundable in many Eastern European countries, the United Kingdom and Canada. According to Morion, the consumption of this drug in 2019 in the hospital sector was 37 units. in the amount of 68.66 thousand UAH, in retail - 3190 unitary enterprise. in the amount of UAH 6.5 million.

At the next stage, the analysis of insulin consumption of different groups was performed. The choice of insulin drugs is made by the doctor taking into account the severity of the disease (in particular, the level of glycemia) and individual characteristics of the patient (lifestyle, diet, ability to ensure frequency of injections and proper monitoring of glycemia) [10].

As a result of the analysis of the dynamics of insulin consumption in the hospital segment in 2015-2019, there is a significant decrease in consumption (in kind and in monetary terms) since 2016, due to the implementation of a pilot project to reimburse the cost of drugs. Thus, in 2017 the number of consumed packages decreased by 2.5 million compared to 2016 (by 62.7%), in 2018 - by another 1.4 million (by 92% compared to 2017). In the retail

segment, on the contrary, consumption has increased more than 10 times over the past 5 years.

The introduction of an electronic register of patients with diabetes made it possible to determine the actual number of patients (currently 203,128 adults and 9,860 children), prescriptions (2,347,000) and the amount of budget funds (UAH 1.47 billion) in Ukraine as a whole. .

The leaders in consumption in the hospital segment in 2019 are fast-acting insulin drugs of the A10A B01 Insulin (human) group (109.5 thousand units and UAH 19.6 million, respectively). In the retail segment, the leading positions are occupied by insulins of medium duration of action A10A C01 Insulin (human) - 1.1 million units. in the amount of UAH 437.5 million.

According to the Reimbursement Program "Available Medicines" as of October 1, 2021, 60,10746 prescriptions were issued during 2019-2021, of which 4.1 million for metformin, 1.8 million for gliclazide, 96.26 thousand for glibenclamide. The largest number was issued to female patients 27999690 prescriptions, male - 1320379, respectively. The largest age group of prescriptions was 65+ - 58.6%, the smallest - 18-39 years (0.79%). In the group aged 40-64 years, the number of prescriptions reached 38.97%, respectively.

The analysis on the basis of territory established that the leaders in terms of the number of discharged were Dnipropetrovsk, Kharkiv and Lviv regions. The smallest number of prescriptions was observed in Luhansk, Chernivtsi and Kherson regions.

As noted earlier, the current model of pricing and reimbursement of insulin drugs in Ukraine has certain shortcomings and needs to be improved, first of all, in the direction of developing a unified methodology of reference pricing for drugs of domestic and foreign production. Approaches to reimbursing the cost of insulin drugs also need improvement.

As part of the study, an external review of wholesale prices for 107 insulin drugs by trade name (per 1 IU) was conducted. According to the current procedure for calculating the reference price (reimbursement price) for insulin preparations (order of the Ministry of Health of Ukraine dated 13.04.2016 №359), the reference countries are: Bulgaria, Moldova, Poland, Slovakia, Czech Republic,

Latvia, Serbia and Hungary. In addition to these countries, insulin prices from available sources in Lithuania, Greece, Kazakhstan, Denmark, and Romania were further investigated.

We have identified the main criteria for the distribution of insulin drugs into reference groups: 1) ATX code (according to the ATX classification, insulins are divided by INN and duration of action), 2) form of release (vials, cartridges and syringe pens). There were 26 reference groups, according to which the analysis was performed.

At the same time, the lowest prices for insulin are most often observed in Hungary - 16 trade names (35.5%), Romania - (31%), Slovakia - (22%), Greece - (17.7%), Poland and Kazakhstan (15), 5%, the Czech Republic - (9.2%), Moldova - (4.4%), Bulgaria - (2.2%). This must be taken into account when choosing reference countries.

Thus, according to the results of the analysis, we propose the following reference countries: Hungary, Romania, Slovakia, Greece, Poland, the Czech Republic (main), Bulgaria, Latvia, Kazakhstan (additional).

Conclusions

In order to improve the system of pharmaceutical support for patients with type I diabetes, a comprehensive study was conducted, the ultimate goal of which was to improve approaches and develop a generalized model of reference pricing for insulin drugs. External review of prices for 107 insulin drugs in 13 countries. A detailed analysis of approaches to determining reference prices and reimbursement of insulin costs in each of the countries selected for analysis. Substantiated methodological approaches to improve the methodology for determining reference prices (prices for reimbursement for insulin drugs).

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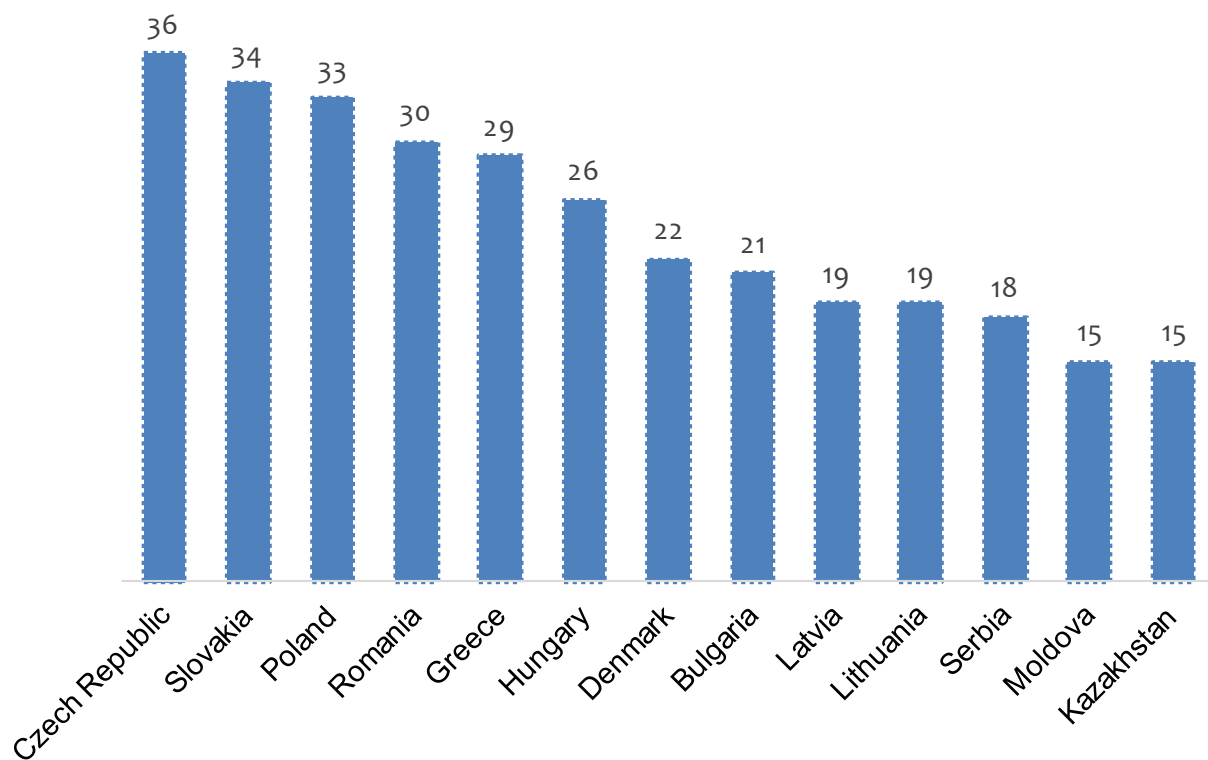


Figure 1. Criteria for selecting reference countries