

Financial Analysis of the Access to Pharmacotherapy for Rare Diseases in Bulgaria

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Abstract

The absence of adequate national strategies for rare diseases (RD), high medicines prices and insufficient experts' knowledge creates the barriers in therapy, as well as the added factors of inappropriate diagnostics and difficulties in peoples' access to health care. A heavier burden is placed on patients' physical, mental, psychological and intellectual wellbeing as well as on the financial capabilities of the third party payers. This study aims to analyze the financial flow for RD therapy as part of the health insurance budget and regional differences in their financing. The point of view is that of the third party payer for a 4-year period. The study is a macro costing top down financial analysis of the expenditures for medicines for rare diseases spent by the 3rd party payer, in Bulgaria that is the national health insurance fund (NHIF). Applied were financial and statistical analyses towards the budget data for expenditures for pharmaceuticals at national and regional level. Results show a constant rise in healthcare medicines expenditures, including those for rare diseases therapy from 20 to 27 million € for a three-year period but it is not above 10% from the budget for medicines due to regulatory restrictions. A variety of deviations exist among regional counties, accounting for more than 50% differences in payment per diagnosis. This could be explained with insufficient knowledge and lack of therapeutic standards. There is a need for collaboration on a European level and the creation of a global fund to be able to satisfy therapeutic needs. A closer look at national differences and regional therapy is necessary, as well as standardization of health care services for better health care expenditures management.

Keywords

Healthcare Budget, Medicines Budget, Rare Diseases, Orphan Medicines

1. Introduction

Rare diseases (RD) have a potentially lethal exit, or are chronic highly debilitating diseases with limited spread and high degree of complexity [1]-[4]. Approximately between 5000 and 8000 different rare diseases affect near 6% of the European population according to the current state of the art scientific knowledge [4]. In Europe it is estimated that 15 million of the inhabitants are suffering or will suffer from RD. As chronic, progressive and degenerative states, they leave patients handicapped for their entire life. Without therapy patients are destined to remain severely injured. In 2008 the European patients' platform (EURORDIS) started an initiative to increase awareness in the society to the problem of RD, their late diagnosis and insufficient therapy information [4]. In June 2000 the same organization established significant discrepancies in the financial and physical access to medicines. The latter was supported by other scientific works, especially in Central and East European Countries showing that the access to orphan medicines for rare diseases therapy is hampered [5]-[7].

The absence of adequate national strategies for RD, high medicines prices and insufficient experts creates to the barriers in therapy, inappropriate diagnostics and difficulties in peoples' access to health care [8] [9]. A heavier burden is placed on patients' physical, mental, psychological and intellectual wellbeing as well as to the financial capabilities of the third party payers.

This study aims to analyze the financial flow for RD therapy as part of the health insurance budget and regional differences in their financing. The point of view is that of the third party payer for 4-year period.

2. Materials and Methods

2.1. Financial Analysis

The study is a macro costing top down financial analysis of the expenditures for medicines for rare diseases spent by the 3rd party payer. In Bulgaria that is the national health insurance fund (NHIF). The analysis covers the period 2010-2013 year.

The information analyzed was collected from the national yearly financial reports of the healthcare budget. The expenditures for rare diseases and pharmaceuticals paid by the NHIF were systematized per diagnosis, per patient and per region. The international classification of diseases (ICD) 10 was used.

Regional cost differences and index changes were calculated. The cost structure was analyzed by diseases, average on patient and by country regions.

2.2. Statistical Analysis

Descriptive statistic and t-test was performed towards the data for the average cost per disease, per patient, and for regional cost differences were. ANOVA analysis was performed to test the statistically significant differences and influencing factors.

3. Results

3.1. Results of the Financial Analysis

Since 2011 the pharmacotherapy cost of rare diseases is paid by the Ministry of health through a national program for RD with the exception of the therapy for 3 diseases—acromegaly, pulmonary hypertension, and phosphorus metabolism disturbances.

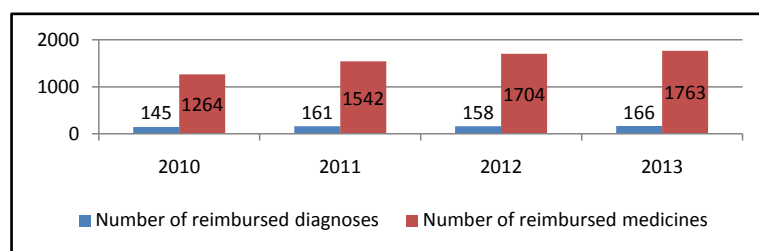
During 2012 the expenditures for pharmacotherapy of rare diseases were reported separately within the health care budget. The financial limit of 10% was imposed on their increase and thus the access to medicines was limited not only clinically, but also financially. Due to these limitations, a decrease in expenditures for medicines was observed as an absolute value in 2012 in comparison to 2011 [10] (Table 1).

In 2013 the expenditures for pharmaceuticals for RD were included into the total health care budget and were not reported separately. The expenditures for oncology medicines were added, due to the fact that their financial responsibility was transferred to the NHIF from the Ministry of health.

It is evident that there is a substantial growth in the health care expenditures for pharmaceuticals, including the RD therapy and all the changes in expenditures are statistically significant ($p < 0.05$). The increase in the expenditures is a consequence of not only the changes in budget policy, but also of the changes in the number of the reimbursed diagnoses and medicines which are constantly increasing (Figure 1).

Table 1. The structure of the NHIF medicines expenditures during 2010-2013 (€).

	2010	2011	2012	2013
Expenditures for medicines, medical devices, and special foods.	196,546,039	241,654,726	265,377,431	273,855,466
Expenditures for medicines	186,734,423	231,397,613	254,752,527	262,843,378
Expenditures for orphan medicines for rare disease therapy		19,969,356	19,918,284	27,068,437

**Figure 1.** Number of reimbursed diagnoses and medicines in 2010-2013.

The transfer of the cost of pharmacotherapy of rare diseases from the Ministry of Health to the NHIF budget in 2011 gave rise to lots of concerns for budget failure due to the fact that there were no planned expenditures in the previously used financial programs. At the same time, it was observed, an increase in the number of covered diagnoses and eligible patients (Figure 2).

The inherited deficiencies in blood clotting factors, thalassemia, pulmonary hypertension, diseases of Gaucher, Fabry, and cystic fibrosis consume the highest part of health care budget spending and affects the biggest part of all patients suffering from RDs Table 2.

According to the anatomy therapeutic classification (ATC) in 2013 the most often reimbursed medicines fell into almost all codes as ATC A (alimentary tract)— $n = 1$, ATC B (blood and blood formulating organs)— $n = 2$, ATC C (cardiovascular)— $n = 1$, ATC G (genito urinary)— $n = 1$, ATC J (anti-infective)— $n = 2$, ATC L (oncology)— $n = 4$, varia V— $n = 1$ (Table 3).

Out of the medicines with orphan drug designation for the therapy of rare diseases are reimbursed medicines with expired orphan drug designation or withdrawn such as shown on Table 4 and Table 5.

3.2. Regional Differences

Regional differences are extremely high. The highest number of patients with thalassemia is in the capital Sofia (region 22; patients $n = 29$), followed by Plovdiv (region 16, patients $n = 25$) the second largest city in the country, but the highest expenditures are paid in Rousse ($n = 6$), and Varna ($n = 3$), where the number of patients is not significant—Figure 3. On average the cost per patient paid by the NHIF at regional level is 17,910 € but differences are between $\pm 14,000$ Euro among all 28 regions and those differences are statistically significant.

For hemophilia patients the average cost per patients is 41,108 € and the regional differences vary among $-16,000$ and $+38,000$ € The highest is the value in region 05 where only 2 patients with hemophilia are treated. Again the morbidity prevails in the two major cities—Sofia (region 22; patients $n = 34$) and Plovdiv (region 16; patients $n = 24$) Gaucher, Fabry and Neyman diseases are classified in one financial group and are the most resource consuming with only 21 patients. The average cost per patient per year of 163,438.29 € and variations are among $+120584$ and -87700 € (Figures 3-5).

Similar are the results for the other rare diseases expenditures with great variations among the regions and with higher deviations in small regions.

Statistically significant are the differences among the number of patients per disease, reimbursed expenditures per region, and per patient—Table 6.

4. Discussion

The budget and regional differences analyses confirm that the therapy of rare diseases consumes a lot of finan-

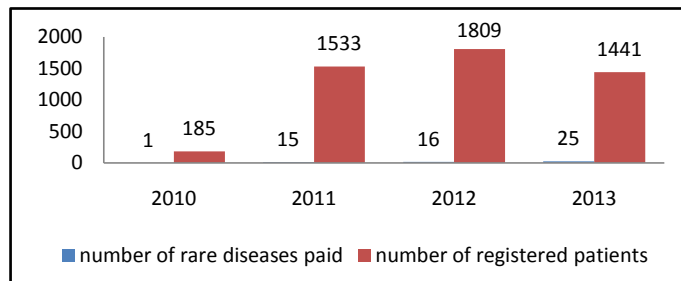


Figure 2. Number of rare disease diagnoses and patients subsidized by NHIF.

Table 2. Number of patients with RD and subsidized sum (€) for their therapy.

ICD code	Diagnosis	2010		2011		2012		Jan-July 2013	
		N of pts	Total sum	N of pts	Total sum	N of pts	Total sum	N of pts	Total sum
D56.1	Thalassemia			219	2,621,348	223	3,914,598	220	2,062,498
D66	Inherited deficiency of factor VIII			226	4,611,618	243	6,862,510	237	4,382,893
D67	Inherited deficiency of factor IX			22	216,214	21	214,230	21	124,503
D68.0	von Willebrand disease			19	232,287	19	228,070	19	209,577
D68.2	Inherited deficit of other blood clotting factors			24	919,167	15	249,156	15	152,522
D80 - D84	Immune system disturbances				0		0	2	2996
E22.0	Acromegaly and hypofysis gigantism	185	24,955	263	597,074	241	1,163,308	243	684,547
E23.0	Hypopituitarism			76	228,110	91	335,561	93	158,912
E75.2	Gaucher, Fabry and Neyman Pick disease			18	2,211,789	21	3,529,122	21	2,011,257
E76	Mucopolissaharoidosis				0	4	426,921	4	816,173
E83.0	Willsom Konovalov			110	15,679	144	39,019	150	20,094
E83.3	Phosphorous metabolism disturbance	22	2725	27	2630	29	2314	29	1466
E84	Cystic fibrosis			179	1,873,550	184	2,331,649	192	1,121,815
I27.0	Lung hypertension	120	1027	126	371,316	126	829,922	131	551,699
P27.1	Perinatal bronchial dysplasia			162	369,712	386	1,459,223	0	1,201,558
Q87.1	Prader Willi syndrome			11	22,724	13	41,876	13	28,410
Q96	Turner syndrome			51	328,384	49	381,180	48	163,855
E74.0	Pompei disease				0		0	2	146,462
E85.1	Amiloidosis				0		0	25	373,671
	Total		2933		14,621,600		22,008,659		14,214,908

cial resources and requires detailed observations and analyses of the medical, humanistic and social reasons for the differences [11]-[13]. Regional differences could be explained with the lack of well-trained personal and specific knowledge for some rare diagnoses [10]. Evidently the lack of medical resources leads to high financial discrepancies which pose a heavy burden on the third party payer. The insufficiency of the well trained staff is also supported by the fact that the discrepancies in financial flows are mainly at regional level. The assumption is that with no knowledge for specific rare diseases the physicians tend to over prescribe unnecessary medica-

Table 3. Most often reimbursed orphan medicines in 2013.

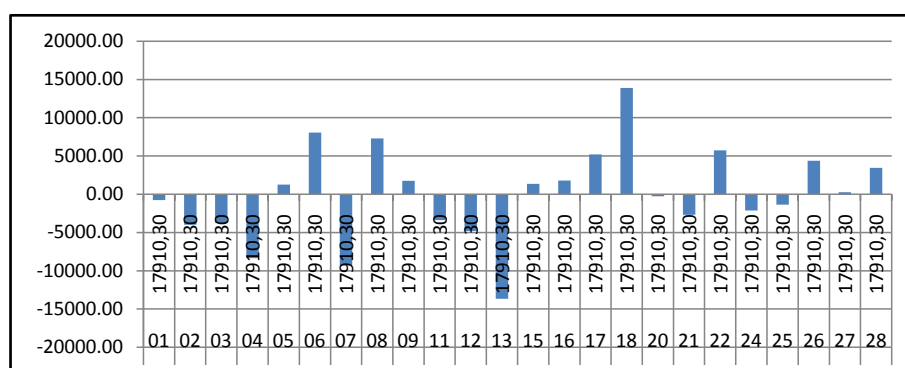
ATC group	International non-proprietary name	Dosage form	Number of packages sold Jan-August 2013	Reimbursed sum (€)
A16AB09	Idursulfase	Sol for inf.	87.00	1,092,416
B01AC11	Iloprost	Nebulaser sol.	30.00	23,076
B02BX04	Romiplostim	Powder for sol. for inj.	717.04	461,998
C02KX02	Ambrisentan	Tabl film coated	34.00	84,049
G04BE03	Sildenafil	Tabl	190.00	99,639
J01GB01	Tobramycin	Nebulaser sol.	213.00	488,392
J01GB01	Tobramycin	Inh power, caps	15.00	37,108
L01XE05	Sorafenib	Film-coatedtabl.	375.63	1,439,816
L01XE06	Dasatinib	Film-coatedtabl.	199.18	784,636
L01XE08	Nilotinib	Caps. hard	4339.21	3,274,735
L01XE09	Temsirolimus	Conc. and solv. sol.inf.	55.20	55,196
V03AC03	Deferazirox	Tabldisp	6528.00	2,516,615

Table 4. Reimbursed medicines with expired orphan designation in 2013.

ATC group	INN	Dosage form	Number of packages sold January-August 2013	Reimbursed sum (Euro)
A16AB04	Agalsidase beta	Powder concinf sol	164.00	1150049.44
A16AX06	Miglustat	Hard caps.	48.00	703694.88
C02KX01	Bosentan	Tabl film coat.	208.00	1091003.68
H01AX01	Pegvisomant	Powder sol inj	34.00	142266.64

Table 5. Reimbursed medicines with withdrawn orphan designation in 2013.

ATC group	International non-proprietary name	Dosage form	Number of packages sold January-August 2013	Reimbursed sum (Euro)
B02BX05	Eltrombopac	Tabl. film coat	454.00	3087014.64
L01XE01	Imatinib	Film-coatedtabl.	590.95	2709839.49
L01XE04	Sunitinib	Caps. hard	425.43	3734256.55
L01XE11	Pazopanib	Film-coatedtabl.	532.76	3190953.30

**Figure 3.** Regional cost differences for patients with thalassemia.

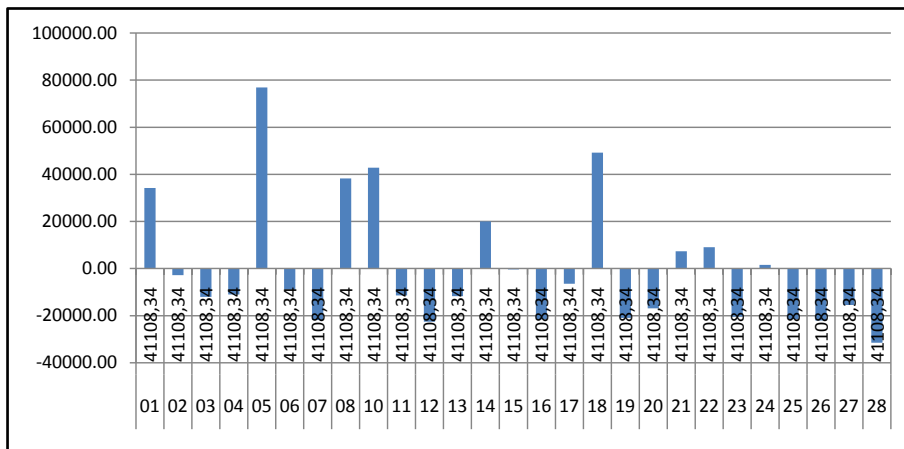


Figure 4. Regional cost differences for patients with hemophilia.

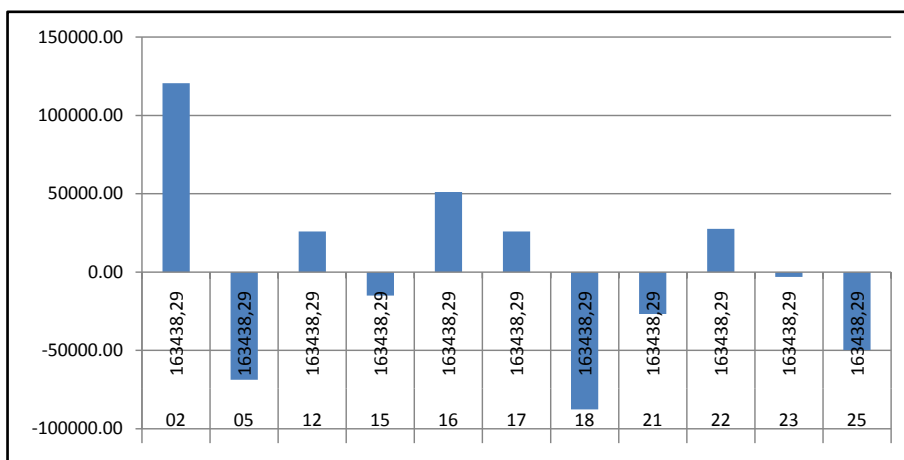


Figure 5. Regional cost differences for patients with Gaucher, Fabry and Neyman diseases.

Table 6. One way ANOVA analysis of statistical differences among the expenditures.

		Sum of squares	Df	Mean square	F	Sig.
Average monthly number of patients	Between groups	3,071,436	27	113,757	5246	0.000
	Within groups	6,266,638	289	21,684		
	Total	9,338,074	316			
Reimbursed Expenditures	Between groups	3.961E12	27	1.467E11	1593	0.034
	Within groups	2.661E13	289	9.207E10		
	Total	3.057E13	316			
Average cost per patient	Between groups	1.479E11	27	5.477E9	0.545	0.970
	Within groups	2.885E12	287	1.005E10		
	Total	3.033E12	314			

tions and thus exceed the financial limits [1]. This is in contrast with other studies revealing that in small cities the prescribing of medicines is usually more restrictive and less costly [8].

Regional differences in financial resources support the need for revision and reasoning of their medical basis. The patients with rare diseases are extremely limited in number but they consume huge amount of the scarce health insurance budget [5]. Every deviation in their therapy should be precisely revised and timely corrected not only to guarantee the necessary medical results, but also to control budget spending. The high expenditures in this group of patients could not always mean better therapeutic results.

5. Conclusions

Within the framework of the very dynamic regulatory environment and extensive scientific work in the field of rare diseases therapy, the financial resources remain extremely limited to ensure appropriate therapy and scientifically based treatment. There is a need of collaboration on a European level and the creation of a global fund to be able to satisfy therapeutic needs.

A closer look at national differences and regional therapy is necessary, as well as standardization of health care services for better health care expenditures management.

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