

Copayment on Drug Prescription and its Influence on Patient Behaviour – a Croatian Example

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The objective of this research is to examine the effects of the changes in medication copayment on prescription with reference to patient support program on a Croatian example. The authors analyse the effects of increasing or introducing copayment to prescription of medicines. The findings show that the introduction of copayment, if the medicine has a generic parallel which is free of charge, noticeably reduces the prescribed volume of medicine for which the copayment was introduced. There has been an observed patients' compliance and it has been shown on the Croatian example that a decrease of copayment through patient support program causes increase in compliance.

INTRODUCTION

Ever-increasing cost sharing has burdened patients with greater share of total spending for health care and medication. Between 2000 and 2009, average copayments jumped from \$8 to \$10 for generic medications, from \$15 to \$27 for preferred medications and from \$29 to \$46 for non-preferred medications in tiered prescription drug plans (Kaiser Family Foundation, 2009). It has been noted that health care costs continue to rise and the burden of chronic disease escalates (Gibson, et.al., 2011). In addition to that, employers must innovate to overcome these impediments to economic sustainability. Croatia is no exception. However, increased cost sharing is intended to reduce the inappropriate use or overuse of medications, as demonstrated in the RAND Health Insurance Experiment (Leibowitz & Manning, 1985).

Lower copayments should result in an improvement in adherence and disease control, and reduction in health care costs. Additionally, copayment reductions generate greater medication adherence in targeted patients (Maciejewski, et.al., 2010). Some researchers showed that tiered prescription copayments were associated with a significant shift from non-preferred to preferred brand medications (Rector, et.al., 2003). Additionally, value-based cost sharing can increase patients' adherence to important medications (Chernew, et.al., 2008).

How does a change in medical copayment influence prescription with reference to patient support program in Croatia? This question was in the focus of the authors which were taken into consideration in this research. Some of them are pointing out that understanding the impact of increase in copayments on medication prescription outcomes has significant relevance, especially in connection with the patient support program (Doshi, et.al., 2009). Additionally, it may also be important to consider ways to create alternative incentives for patients to take medications – even incentives that are more powerful than value-based insurance design (Maciejewski, et.al., 2010). One possibility that has been examined in the context of Warfarin adherence (Volpp, et.al., 2008) and the treatment of substance abuse disorders (Sindelar, et.al., 2007) is paying patients to take medications. There are researches from behavioural economics suggesting that incentives may not be effective if they are too small or if they are too large (Gneezy & Rustichini, 2000; Ariely, et.al., 2009).

CROATIAN BACKGROUND

The Croatian Chamber of Pharmacists is reporting by publishing the data on their official website since 1991 when the privatization of the pharmacy sector has started and new pharmacies were opening in Croatia. About 2.100 pharmacists perform public and 110 pharmacists hospital pharmaceutical activities in 960 community and 52 hospital pharmacies. About 63% of the community pharmacies are privately owned, 23% are state-owned and 14% are privately leased. On average, there are two pharmacists per pharmacy. There are two professional organizations in Croatia: the Croatian Chamber of Pharmacists and the Croatian Pharmaceutical Society. Pharmacists who work in community and hospital pharmacies are responsible for drug supply, dispensing medicines, production and quality control of magistral and official formulas, adverse drug reporting and providing information about medicines for health professionals and to the general population. Hospital pharmacists are not part of the hospital team and they do not work on wards. A system of dispensing unit drug dose therapy was established in Croatia on the cardiac surgery ward in Zagreb's Clinical Hospital Dubrava during 1996, and this systematic clinical practice has shown a significant decrease in drug consumption. In community pharmacies beside basic services, pharmacists provide certain advanced services, as disposal of waste medicines, night services, blood pressure measurement and weight measurement. In addition, the Croatian Health Insurance Fund (CHIF) is publishing on their official website that the health care standard in Croatia is generally satisfactory, with better accessibility to health care facilities in the major cities.

Due to commonly rising costs of health care, especially expenditure on drugs, Croatia's health care system is accompanied by a lack of budget funds for health care, which so far has not affected drug supply within the public health care institutions in Croatia. The Croatian Ministry of Health plays the role of the system controller, with a wide scope of authority. This entails managing the health care legislation, proposing budgetary expenditures, monitoring health condition and health needs of the population, education of the health care workers and supervision of the health care system reform efforts in Croatia. As part of its management role, the Ministry was assigned to draft and implement the National Health Care Strategy for the period 2012-2020. The health care reform in Croatia underlies common values and principles, reducing inequality among the Croatian citizens. Strategic development directions of the health care system entail improved interconnectivity and continuum of health care, standardization of health care quality, improving efficiency and performance of the system, increasing the availability of health care and improving health indicators.

The Croatian health care system is financed through several sources. Health care contributions in Croatia are mandatory for all employed citizens, i.e. their employers. The dependents obtain their health care coverage through contributions paid by working members of their families. Self-employed workers in Croatia are also obliged to pay health care contributions. Croatian citizens who belong to a particularly vulnerable category are exempt from paying health care contributions; retired people and persons with a low income are insured and have access to health care facilities - contractual partners - of the Croatian Health Insurance Fund (CHIF). Croatian citizens have the option to obtain health services within private health care providers which are not CHIF contracted partners, either through direct payment or through supplemental insurance which is covering the payment.

Croatian citizens are required to participate in health care expenditures, except for certain categories of insured persons (e.g. children under age of 18) or insured persons suffering from certain diseases, when the health care services are being rendered due to complications caused by the diseases (e.g. malignant diseases or chronic mental illnesses). For some health care services, such as plastic surgery, insured persons are obliged to pay by themselves, i.e. the cost is not being covered by their mandatory health insurance. Family doctors (GP) suggest the patient's further treatment in secondary or tertiary health care service if needed, which enables the patient free access to hospitals and polyclinics which have signed contracts for rendering health care services from mandatory health insurance (contractual partners).

Health care services on the secondary and tertiary level in major cities are mainly rendered in hospitals. Hospitals can be classified as clinical, general and special hospitals. General hospitals have organized activities that include OBGYN, internal medicine, surgery and paediatrics. After joining the EU in 2013, Croatia is able to utilize funding from the EU structural funds for the development of the health care sector. This is supposed to financially strengthen the Croatian health care system by extra funding intended for improving the health care sector and rendering health services to Croatian citizens.

Although currently undergoing a reform, the Croatian health care system is rendering health care services in accordance with the European standards. Access to health care outside major cities is fairly reduced, but this mainly concerns outpatient-conciliar health care, while primary health care and emergency medicine are available in all parts of the country. Today, there are 30 active pharmaceutical companies in Croatia. Of this number, the 10 largest pharmaceutical manufacturers were responsible for 30% of the total industry's income in 2013.

According to the data available in the IMS database, in the past four years the consumption of prescription drugs declined by 449.982.380,34 HRK which is a significant sign of price pressures by the insurers and of striving for additional medication control. Table 1 shows the list of the reference countries in Europe for the calculation of the drug price.

TABLE 1
LIST OF THE REFERENCE COUNTRIES IN EUROPE FOR THE CALCULATION OF THE DRUG PRICE (INTERNATIONAL PRICE REFERENCING)

	Bulgaria	Romania	Turkey	Croatia	Latvia	Hungary	Poland	Lithuania	Estonia	Slovak Republic	Portugal	Greece	Czech Republic	Slovenia	Malta	Cyprus	Spain	Italy	United Kingdom	France	Iceland	Finland	Belgium	Germany	Denmark	Sweden	Netherlands	Ireland	Austria	Switzerland	Norway	Luxemb...		
Bulgaria																																		
Romania																																		
Turkey																																		
Croatia																																		
Latvia																																		
Hungary																																		
Poland																																		
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Estonia																																		
Slovak Republic																																		
Portugal																																		
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Czech Republic																																		
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Malta																																		
Cyprus																																		
Spain																																		
Italy																																		
United Kingdom																																		
France																																		
Iceland																																		
Finland																																		
Belgium																																		
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Ireland																																		
Austria																																		
Switzerland																																		
Norway																																		
Luxembourg																																		

STUDY DATA AND METHODS

Although the literature examining the effects of copay changes on utilisation is extensive (Goldman, et.al., 2007; Gibson et.al., 2005), in this study the authors evaluated and examined the effects of the changes in medication copayment on prescription with reference to patient support program. There are several reasons why we might expect an impact of copay lowering or copay increasing on prescription. Although some authors studied a population of patients who may be particularly sensitive to relatively small absolute changes in copayment levels, their results are very consistent with those of the other healthcare environments (Doshi, et.al., 2009). The data demonstrates that copayments, which are intended to reduce the less important or „discretionary“ services by making patients responsible for part of their costs, also adversely affect the use of therapies that may be considered „essential“ (Choudhry, 2009). Some authors are concluding that there are several reasons why we might expect the impact of copay-lowering schemes to differ from copay-raising initiatives (Chernew, et.al., 2008). Specifically, with the latter, employees are losing something by being forced to pay more. With the former, they are being given something - lower copays. Although neoclassical economics suggests similar but opposite effects associated with increases versus decreases in copay rates, considerable research in behavioural economics suggests that the results might not be symmetrical because of employee anchor points and, perhaps, endowment effects (Camerer, 2000).

The pharmaceutical industry belongs to the most important and influential industries nowadays in the Republic of Croatia. In addition to the Croatian Health Insurance Fund, there are several private health insurance companies where citizens can pay for supplementary health insurance policies. Still, the Croatian Health Insurance Fund covers compulsory insurance as well as medication copayment list and levels of payment.

In this paper the authors aimed to find a correlation between the decrease of copayments on some medicaments and lowering of its prescription, as well as the lowering of its final sales in Croatia. With this knowledge, the authors believe it could be possible to develop a further pricing strategy within the pharmaceutical companies which could be further developed in two possible directions: either to allow internal medication price lowering or to approve certain patient support programs in order to make those medications affordable to the end-users. From the insurers' perspective, those examples could help in the estimation of long-term affordability of certain medical therapies or connection between final cure outcomes with pricing structure and/or copay of certain medicament.

Most of the literature either compares adherence across firms with different copay rates or examines the effects of copay increases. However, several authors are suggesting that because of concerns about the adverse clinical effects of high copayment rates, several large employers have reduced these rates for selected high-value services and there has been limited evaluation of these copay declines (Freudehneim, 207; Fuhrmasn, 2007; Ridley, 2005; Landon, et. al., 2007). The CHIF budget available for drugs is getting lower and lower year-on-year. The budget was 40% lower in 2014 compared to 2013 and in 2015 5% lower compared to 2014. This is followed by its natural circumstances in connection with the copayments rates. Based on these facts, the authors assume that the patients in Croatia are very sensitive to any change in medication copayment. If they have until now used a kind of drug without copayment which will lose this status and it is supposed from the patient to cover a part of the drug's price, prescription as well as consumption of that drug will be significantly lower than in the previous period without any copayment. The sales of this drug will be significantly lower and the Croatian patients will rather decide for an alternative therapy, drug and/or medical treatment. This means that they decide to take a drug without copayment as their final choice. The authors closer follow the level of cooperation of the patients in the drugs taking process, as well as its correlation with the therapy copayment rate. The final objective is to define the influence of copayment drug price change on its prescription and final sales, as well as on the cooperation among patients. The research consisted of primary and secondary research methods. Primary research includes analyses and comparisons between two databases: the IMS database (selling base) and the database of the patient support program called „Narančasta kartica“

(Orange Card). Secondary research includes an analysis of available literature and articles published on the topic of copayment and its influence on patient behaviour.

The following hypotheses are formulated to guide the study:

(H1) Introducing of copayment will lower consumption of the drug in comparison with other drugs within the same drug category.

(H2) The abolition of copayment on inhalation therapy affects better patient compliance.

RESEARCH AND ANALYSIS

The compulsory drug list specifies the drugs with prices on the level of the reference price or lower, while the supplementary drug list specifies the drugs with prices higher than the reference price. This means in practice that the same group of reference can contain the original drug (such as Seretide Inhaler 250), as well as a generic drug (such as Duohal Inhaler 250 mcg). During the research period both drugs were part of the basic drug list without any copayment for the patients. According to the rules of the CHIF, generic drugs used to be 30% cheaper compared to the original drug. During the therapeutic price referencing (TRP) process, in case that Duohal reaches an average volume bigger than 5% within this group within a three months period, the price which CHIF will be paying for the original drug will be the same as the price paid for Duohal (200,21HRK plus VAT) to the original drug authorisation holder, in this case GlaxoSmithKline (hereinafter: GSK), meaning two things:

1) It will lower the drug price from 286,02 HRK to 200,21 HRK which means it has to get internal approval for price lowering to this level and be aware of the IRP process for other countries in Europe which refers on prices listed on the Croatian pricing lists;

2) It will keep the drug price and be transferred to the supplementary drug list where CHIF has to pay 200,21 HRK and the patient has to pay the difference of 85,81 HRK plus VAT which equals the full price of the drug.

As part of this research, the authors have taken an example and analysed the drugs Salmeterol+ Flutikazon in the Croatian inhaler market and Amoxicilin + Klavulanacid in the Croatian pills market. According to the data available on the CHIF official website, after 28th February 2015, i.e. after the therapeutic referencing drug process (TRP), some drugs, among them the already mentioned Salmeterol + Flutikazon, as well as Amoxicilin and Klavulan acid, have been transferred from the basic drug list with zero copayment to the list of drugs where the patient's copayment is expected. For some of the drugs the copayment level has been raised, as well. Copayment for the Seretide 50 Inhaler has been raised from 14,62 HRK including VAT to 64,89 HRK including VAT, while the Seretide 250 Inhaler got copayment in amount of 85,81 HRK including VAT, as well as for Klavocin which costs the patient 17,42 HRK including VAT. It has to be taken into consideration that the Salmeterol + Flutikazon therapy belongs to chronic therapy while Amoxicilin and Klavuran acid therapy belongs to acute therapy.

DESCRIPTION OF PATIENT SUPPORT PROGRAM

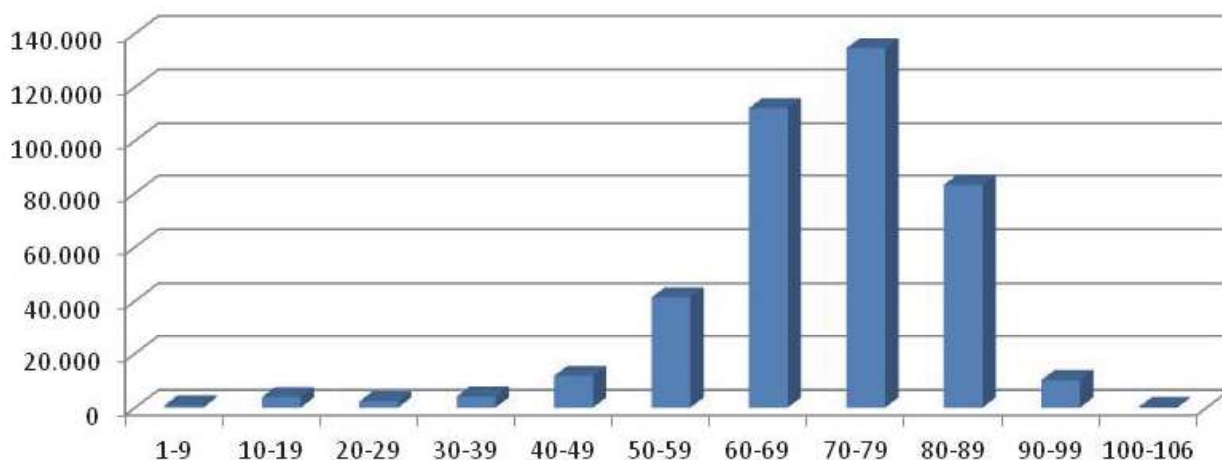
Additionally, the authors have taken into consideration and into additional analysis the only existing patient support program in this form on the Croatian market, the socially responsible program known in Croatia under the name „Narančasta kartica“ (Orange Card), completely subsidized by the company GlaxoSmithKline d.o.o. The program makes drugs with copayment more accessible to the Croatian patients, so that GSK bears for the patient a part or even the entire amount of copayment for some of their drugs. The program is active since December 2013 and represents a new practice in the Croatian market. For the time being, the program is available in more than 90% pharmacies in Croatia, and could be developed into a customer loyalty program, offering additional benefits to the patients, as well as a competitive advantage to the company and possibly the development of further CRM activities.

Customer loyalty presents a paradox. Many see it primarily as an attitude-based phenomenon that can be influenced significantly by customer relationship management initiatives, such as the increasingly popular loyalty and affinity programs (Uncles, et.al, 2003). Some define loyalty as an ongoing propensity

to buy the brand, usually as one of several (Ehrenberg & Scriven, 1999). An intense interest in customer relationships is also apparent in marketing practice and most evident in firms' significant investments in customer relationship management (CRM) systems (Kerstetter, 2001; Reinartz & Kumar, 2002; Winer, 2001). Customer retention rates and customer share are important metrics in CRM (Hoekstra, et.al., 1999; Reichheld, 1996) and the principle of CRM is to focus efforts on the most loyal customers (Verhoef, 2003).

Thus, developing programs such as „Narančasta kartica“, offered by the company GSK on the Croatian drug market, can serve, among additional issues, for this particular purpose. On the other side, the past decade has seen many firms (re)adopting customer focus – often through a formal program of customer relationship management (CRM). Examples of such practice are provided by many authors such as (Brown, 2000; Kalakota & Robinson, 1999; Peppers & Rogers, 1997). During the period from the beginning of the program introduction till end of June 2016 (01.12.2013 – 30.06.2016), according to the GSK database (2016), it was possible to observe that the total number of transactions reaches figures of almost 432.000. Out of that number, 50% transactions are transactions of female beneficiaries. Additionally, it was possible to follow the number of transactions according to age groups, as well as some other important segmentation variables (such as geographical dispersion, etc.)

FIGURE 1
NUMBER OF TRANSACTIONS IN THE PERIOD 01.12.2013 – 30.06.2016 ACCORDING TO THE PATIENT'S AGE STRUCTURE



Basic Information about the Drugs Market to Treat Respiratory Diseases in Croatia (R03 Market)

The R03 market got its name according to the ATC classification (Anatomical Therapeutic Classification) and it covers drugs intended for the treatment of respiratory diseases, such as asthma and chronic obstructive pulmonary disease. The period analysed for the purposes of this research includes 24 months (June 2014 – June 2016). Subject of observation were the shares of groups of different drugs in June 2016, according to the most recent IMS report from the IMS database (2016). The R03 market alone has lost within the analysed period almost 70.000 drug boxes, resulting in a market decline of almost 4%.

TABLE 2
R03 MARKET IN THE PAST 24 MONTHS – RATE OF GROWTH AND CHANGE IN
ABSOLUTE VOLUMES – COMPARING PERIODS OF LAST 12 MONTHS (JULY 2015 – JUNE
2016) WITH 12 PREVIOUS MONTHS (JULY 2014 – JUNE 2015)

Name	Growth/decline absolute volume	Growth/decline in %	Evolutionary index
GLUKOKORTIKOIDS	-5.576	-3.71%	100
ICS/LABA	-5.402	-1.13%	103
KSANTINI	-30.039	-10.48%	93
LABA	-3.311	-5.75%	98
LAMA	20.178	-6.86%	111
LAMA/LABA	19.979	645.11%	773
OTHER	-14.790	-6.89%	97
SABA	-49.199	-13.52%	90
SAMA/SABA	565	56500.00%	58.748
R03 MARKET	-67.586	-3.66%	100

Review and Analysis of the Volume Fraction of the Drug Depending on a Surcharge Drug

The analyses of the databases has shown that cost referencing, mainly therapeutic price referencing (TRP), can influence a particular drug migration from the basic to the non-exclusive list. In other words, drugs copayment growth changes the drug's competitive market position. In any way, drug competitiveness cannot be seen only through its price or copayment level; it has much to do with numerous promotional and marketing activities led by the company. One such example provides the patient support program „Narančasta kartica“.

An analysis has been carried out of the dependence of the drug price and its market volume before and after the copayment introduction. An analysis has been carried out of the volume of the Duohal Inhaler 250 mcg and Seretide 250 Inhaler drugs before and after March 2015, taking into consideration the moment when the drug price was changed, i.e. when CHIF has lowered the part which it covers to the level of the Duohal Inhaler's 250 mcg drug price. In this period, the Seretide 250 Inhaler has moved to the supplementary drug list and got copayment before and after March 2015 in the amount of 85,81 HRK including VAT. At the same time, Seretide 250 Inhaler has been included into the patient support program „Narančasta kartica“. This means that all the users of „Narančasta kartica“ from this moment on were paying for Seretide 250 Inhaler 29,99 HRK including VAT in all pharmacies which are part of the program. Duohal Inhaler 250 mcg is a drug without copayment.

When comparing the data, it became evident that in the months before therapeutic price referencing the Seretide 250 Inhaler has held more than 70% of the relevant market. But after March 2015, this percentage has been drastically lowered. In June 2016, the volume share of Duohal Inhaler 250 mcg was only 59%.

Additionally, the data analysis has shown that many „new patients“, thus patients who previously did not take this drug, are now using the „Narančasta kartica“ program on a monthly basis and become program members.

When analysing and comparing the period of 6 months before and after the copayment introduction, it became evident that the market has fallen in volume by 25% and Seretide 250 Inhaler by 54%, while the Duohal Inhaler 250 mcg drug has grown by 114%. One of the reasons is the change in copayment.

An analysis has been carried out of the therapeutic group for the MDI Inhalers salmeterol + flutikazon50 mcg, i.e. of the group consisting of the Duohal Inhaler 50 mcg and Seretide 50 Inhaler, taking into consideration the month when the price change took place, i.e. the month when CHIF has lowered the part it is paying on the Duohal drug price. At that moment, the copayment for Seretide 50 Inhaler jumped from 14,62 HRK including VAT to 64,89 HRK including VAT. The drug was than

included in the patient support program „Narančasta kartica“. From this moment on, all the users of „Narančasta kartica“ pay the amount of 29,99 HRK including VAT for the Seretide 50 Inhaler. Duohal Inhaler 50 mcg is offered without copayment.

After the data comparison, it became evident that in the months before the therapeutic price change the Seretide 50 Inhaler had more than 70% of the relevant market. After March 2015 the market share was on average lowered only by some 10%.

By analysing the number of the „new patients“, thus of the patients who earlier did not take this drug using the „Narančasta kartica“ program and who are now becoming program members on a monthly basis, during the observation periods of 6 months before and after the copayment introduction, it became evident that the market has fallen in volume by 6%, the Seretide 50 Inhaler by 25%, while Duohal Inhaler 50 mcg has grown by 90%. This case is somewhat different in comparison with the previous case.

The assumption is that the patients have paid before the copayment for the drug Seretide 50 Inhaler, so that the copayment increase, especially if the drug is used as part of the „Narančasta kartica“ program, hasn't caused a switch to free treatment, i.e. to Duohal.

Analysis of Development of the Drug Volume after Copayment Introduction Trough Time

Taking a closer look at Table 3, it becomes evident that during the observed period of 28 months, i.e. 14 months before price referencing (January 2014 – February 2015) and 14 months after price referencing (March 2015 – June 2016) Seretide has lost more than 17.000 boxes, while Duohal got 14.429. Percentage-wise, this means a drop of 42% and a growth of 227%, respectively.

TABLE 3
COMPARISON OF INCREASE/DECREASE IN VOLUME THROUGH COMPARISON PERIOD OF COPAYMENT INTRODUCTION FOR SERETIDE INHALERS OF 14 MONTHS (MARCH 2015 – JUNE 2016) WITH PERIOD OF 14 MONTHS BEFORE COPAYMENT INTRODUCTION (JANUARY 2014 – FEBRUARY 2015)

Drug Name	Increase/Decrease of absolute drug volumes	Increase/Decrease in %	Evolutionary index
Duohal Inhaler 250 mcg	13.292	234%	356
Duohal Inhaler 50 mcg	1.137	168%	286
DUOHAL total	14.429	227%	348
Seretide 250 Inhaler	-16.818	-46%	58
Seretide 50 Inhaler	-566	-11%	95
SERETIDE total	-17.384	-42%	62

How long did it take until the volume of the Duohal Inhaler 250 mcg outran the volume of the drug Seretide 250 Inhaler? The first equalizing in volume happened at the very moment when the original drug was transferred to the supplementary list (March 2015) and finally taking top place in this market, Duohal Inhaler 250 mcg has reached from September 2015 onwards. It is clear that a large number of patients who have used the Seretide drug before have started to use the Duohal drug.

Impact Analysis of Drug Copayment Lowering Using Patient Support Program on Patient's Compliance

The sensitivity of the market on copayment change has been observed on the drug RelvarEllipta which is manufactured by GlaxoSmithKline. The drug is available in two variants: 92/22 mcg and 184/22 mcg. In the smaller dosage it is indicated for treatment of asthma and KOPB and in the larger dosage for

the treatment of asthma only (GSK database, 2016). It is, as well, the latest drug on the ICS/LABA market and the only one which is administrated within one day.

Table 4 shows that both drug doses are part of the „Narančasta kartica” patient support program with a patients’ copayment level of 29,99 HRK including VAT. This copayment was valid until 17.11.2015. In order to improve the availability of the drug to all the patients, the level of copayment was abolished with the „Narančasta kartica“ patient support program.

TABLE 4
LEVELS OF COPAYMENT WITHIN THE “NARANČASTA KARTICA” PROGRAM FOR THE RELVARELLIPTA DRUG TILL 17.11.2015

Non-proprietary drug name	Appr. holder	Protected drug name	Shape, strength and pack. of drug	Price in HRK for origin. pack. incl. VAT	Price in HRK for original pack. incl. VAT, paid by CHIF	Copayment in HRK for original pack. incl. VAT	Amount in HRK including VAT covered by the „Narančasta kartica“ program	Copayment level in HRK including VAT for patient after using the „Narančasta kartica“
Flutikazon fluorat + vilanterol	Glaxo Operations UK Ltd.	Relvar Ellipta	Inhaler powder 30x(92+2 2 mcg) dosage	314,62 HRK	257,42 HRK	57,20 HRK	27,21 HRK	29,99 HRK
Flutikazonfluorat + vilanterol	Glaxo Operations UK Ltd.	Relvar Ellipta	Inhaler powder 30x(184+22 mcg) dosage	328,92 HRK	257,42 HRK	71,51 HRK	41,52 HRK	29,99 HRK

Considering the market and drug volumes, the decision of GSK was to set the copayment amount as part of the „Narančasta kartica“ program from November 2015 to 0,00 HRK for the patients, thus the company subsidizes the total copayment amount of 57,20 HRK for the smaller dosage and 71,51 HRK for the larger dosage for RelvarEllipta (see Table 5).

TABLE 5
LEVELS OF COPAYMENT WITHIN THE “NARANČASTA KARTICA” PROGRAM FOR
RELVARELLIPTA AFTER 17.11.2015

Non-proprietary drug name	Approval holder	Protected drug name	Shape, strength and pack. of drug	Price in HRK for original pack. incl. VAT	Price in HRK for original pack. incl. VAT, paid by CHIF	Copayment in HRK for original pack. including VAT	Amount in HRK incl. VAT covered by Narančasta kartica program	
Flutikazon fluorat + vilanterol	Glaxo Operations UK Ltd.	Relvar Ellipta	Inhaler powder 30x (92+22 mcg) dosage	314,62 HRK	257,42 HRK	57,20 HRK	57,20 HRK	0,00 HRK
Flutikazon fluorat + vilanterol	Glaxo Operations UK Ltd.	Relvar Ellipta	Inhaler powder 30x (184+22 mcg) dosage	328,92 HRK	257,42 HRK	71,51 HRK	71,51 HRK	0,00 HRK

After 17.11.2015, the copayment for all patients who were taking the RelvarEllipta drug using the „Narančasta kartica“ program equalled 0,00 HRK. After that, the sale of both dosages of the RelvarEllipta drug has grown. The analysis of the data from the „Narančasta kartica“ database has shown that before 17.11.2015 33% of the patients who were taking RelvarEllipta using the „Narančasta kartica“ program have taken one or two drug boxes, never coming back for another dosage. This amount was lower and in the period 17.11.2015 - 30.06.2016 equalled 27%, which means that the patients give up their therapy to a lesser extent and they continue using the therapy after one or two boxes.

The authors also observed the patients' compliance despite the short period of time which was used for observation. The patients' compliance was reduced to the regular use of the drug within the observed period. The analysis excluded all patients who gave up therapy, as explained earlier in this paper, because they represent, by definition, uncooperative patients. It has been shown that patients' compliance was 69% in the period before 17.11.2015, while after 30.06.2016 it equalled 79%. According to the data available on <http://www.social.eyeforpharma.com/column/adherence-and-patient-support-programs>, in May 2016 it has been estimated that the lack of therapy compliance in the USA equals around 300 million USD within the medical costs which can be avoided, while in Europe the lack of therapy compliance is responsible for 200.000 deaths on an annual basis, representing costs for the overall economy of 125 billion EUR. This figure is growing year to year.

Besides all that has been mentioned, it is possible to recognize, after the data analysis, that during the period after November 2015 the number of new patients joining the „Narančasta kartica“ program increased each month. Before this period, the program registered approx. 120 new patients each month. After the copayment repeal, the program was joined on average by 330 patients each month. Researches conducted by several authors have shown that during such pricing interventions therapy adherence by patients went up from 7% to 14% (Chernew, et.al., 2008; Gibson, et.al., 2005). All this speaks in favour of the fact that the main barrier for more regular drug consumption, as well as for drug's prescription, was nothing but drug copayment which was eliminated with the „Narančasta kartica“ program mechanism.

Analysis of the Influence of Copayment Introduction on the Volume Shares in the Antibiotic Market

This part of the analysis includes another case which clearly shows how much the Croatian market is receptive and sensitive to changes on the copayment level. The drugs belonging to the amoxicillin and klavuran acid market have been available to the patients free of charge until 28.02.2015. Basically, they have been part of the basic list of drugs. In the period between 20.02.2015 and 17.11.2015, only the Klavocin drug has been available on the supplementary drug list, with copayment in the amount of 17,42 HRK including VAT. Taking a closer look at the IMS database (2016), the authors were able to identify the size and potential of the copayment influence on sales and on the Klavocin drug market volume on this market.

TABLE 6
DRUG VOLUMES IN THE AMOXICILIN + KLAVURAN ACID MARKET ON A MONTHLY BASIS

	Augmentin	Medoclav	Klavophar	Klavocin	Klavobel	Klavax	Clavius
July 2014	11.675	93	10.188	10.022	7.640	2.624	
August 2014	7.906	297	13.008	58.666	8.662	3.138	
September 2014	21.082	729	17.772	56.417	10.542	7.338	
October 2014	15.560	936	18.706	13.051	10.291	7.952	
November 2014	10.554	557	12.861	90.492	8.416	8.354	
December 2014	8.203	124	12.761	25.368	10.102	5.446	
January 2015	13.174	114	16.719	19.628	10.129	3.701	
February 2015	13.001	90	16.243	97.745	11.863	12.513	
March 2015	10.543	119	14.850	16.876	5.853	5.648	
April 2015	20.453	150	11.944	5.948	22.835	4.931	
May 2015	17.129	76	7.569	9.274	13.937	15.656	
June 2015	17.585	201	6.400	25.842	14.538	11.743	
July 2015	20.150	133	8.002	13.161	14.803	16.484	
August 2015	11.291	234	6.733	17.486	17.120	5.034	
September 2015	1	704	33.046	44.504	13.585	12.700	
October 2015	13.481	870	19.902	13.337	13	10.490	
November 2015	14.317	190	10.860	65.764	2	19.549	
December 2015	10.447	19	13.642	41.940	1	12.460	
January 2016	24.544	84	12.159	36.843		676	3.206
February 2016	10.024	52	6.722	59.025		1.040	6.755
March 2016	5.023	58	6.765	60.859	381	3.382	6.371
April 2016	6.915	44	-5.818	39.060	5.762	838	8.652
May 2016	9.261	47	230	56.056	7.728	1.371	5.568
June 2016	7.797	447	90	51.978	6.429	8.489	5.861

CONCLUSION

The research has proven both hypotheses from this research study. The introduction of copayment lowers consumption of the drug in comparison with the other drugs within the same category of drugs. The abolition of copayment on inhalation therapy affects better patient compliance. The copayment increase heavily impacted medication prescription. It has been shown on the example of the Seretide and Duohal drugs how the copayment introduction lowers the level of drug consumption as compared to the other drugs without copayment within the same group of drugs. It has been shown on the example of the RelvarEllipta drug how drug copayment repeal using patient support program influences patients' compliance. Despite the pressures on drug pricing, the therapeutic outcome for each patient should be taken into account. If increasing or introducing copayment means poor control of diseases or situations when the patients do not adhere to the prescribed therapy, in such cases the pharma-economic benefit

should be assessed, i.e. the pharma-economic risk and/or benefit based on such pricing approach of the insurers, as well as the authorization holders.

If we look from the perspective of the authorization holders, we can conclude, based on the conducted analysis, that in case of therapeutic price refinancing the price retention has a higher negative influence on long-term profit, as well as the introduction of patients' copayment increase in comparison with price lowering and remaining on a basic drug list.

If we look on these cases from the perspective of the insurer - in our case CHIF - in this case all aspects should be taken into consideration what outcome the pricing policy in a long term can have on patients' treatment and try to find the optimal way of balancing between the drug budget and the quality of the service delivered, i.e. the optimal therapeutic outcome for each patient.

Recommendations for further researches exist. In this case, a longer period of time should be taken into consideration, especially when studying patients' compliance. Also, it would be worthwhile to address examples of interchangeable drug groups, but have copayment. It is appropriate to assess whether in this case lower copayment influences drug prescription.

In addition to all of the above, the most valuable database for any future analyses should be the so-called tertiary sales, i.e. the database currently in the possession of the CHIF which is not available to the users outside CHIF. This database could be able to show the real compliance rate of each patient, as well as the sensitivity of certain doctor's segments and the patient's segments on change of or copayment introduction.

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