COMPARATIVE ANALYSIS OF THE MEDICINES
REIMBURSEMENT MODELS IN ITALY, FRANCE, UNITED
KINGDOM, AND GERMANY

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SUMMARY
The aim of this study is to investigate and make a comparative analysis of models of reimbursement of medicines in selected Western European countries, the EU based. Selection of the countries is because they are relatively stable economic members of the G8 and old traditions patterns drug policy, present different reimbursement models and apply any specific mechanisms in the financing of drugs from their public funds. The analysis is based on specific legislation and mechanisms of reimbursement of medicines in those western European countries was examined in the literature databases, legislative bases and national health reports. All countries apply a mix of measures for cost control of the reimbursement. Measures of detention of the costs of drugs in the system of reimbursement and in the 5 countries include positive drug list and a negative one, type of economic evaluation is also used in the five countries as well as schemes for sharing the risk, surcharge of patient and reference pricing. Used more and more standardized methods for systematic assessment and evaluation of criteria such as the relative effectiveness, profitability, budget impact, medical / therapeutic needs, social and ethical considerations also play a role in these decisions.

KEYWORDS: Financing, reimbursement, drug positive list, sharing schemes risk, health technologies assessment.

INTRODUCTION
The public nature of health obliges the state to a consistent policy that aims to ensure the protection of human health in the optimal use of public funds. Decisions in healthcare and in
any other area of human activity, must be economically rational, including those relating to health have a limited character. The financial resources of health are a necessary condition to drive all elements of the system.\textsuperscript{[3, 4,5,6,7,8,9,10,11]} Its main purpose is to obtain a public health impact. Healthcare industry refers to the group of those socio-cultural activities, for which is characteristic that they do not have immediate economic objectives as other sectors of the economy.

Many European countries share the health policy objectives of sustainable development, justice and quality of health care, but the way in which they work, can differ substantially between countries.\textsuperscript{[12,13,14]}

**Member** - States of EU are struggling to cope with the challenge of reconciling different, partly conflicting goals of drug policy related to the reimbursement of medicines, patient access and equity of companies, cost reduction and sustainable funding, and award a prize for innovation of the pharmaceutical industry.\textsuperscript{[15]}

**The main requirements are expected to answer a national pharmaceutical policy are**

1) regulatory framework to ensure good quality of medicines from production throughout the supply chain to the patient;  
2) mechanisms for ensuring equitable access to medicines for the population, especially for vulnerable groups;  
3) strategies that support the financial sustainability of the system to be able to meet the above-mentioned purpose\textsuperscript{[5,16,17]}  

Transparency Directive of the EU, for which the European Commission proposed a revision in 2012 and issued an opinion in March 2013 provides a common procedural framework for decisions on pricing and reimbursement, particularly in terms of time required for making decisions and how these decisions must be communicated and implemented.\textsuperscript{[18,19]} Transparency Directive expressly states that the decision-making process as it is and remains the responsibility of Member States. The way to evaluate medicinal products and their recovery can affect the action of medicines and the application of innovation. Policy in one Member State can affect those of another. For example, the pricing policy in one country can have an impact on parallel trade or foreign official price quoted.
In light of the above, the purpose of this study is a comparative analysis between national models of reimbursement of medicines in selected Western European countries Italy, France, United Kingdom and Germany.

MATERIALS AND METHODS
For conducting comparative analysis of specific legislation and mechanisms of reimbursement of medicines in those western European countries was examined in the literature databases, legislative bases and national health reports. The analysis was structured on the following issues
1. The existence of a positive list
2. The existence of negative list
3. The existence of health technology assessment-HTA
4. Available legislative schemes for risk sharing between pharma companies and institutions paying services
5. Availability of patient co-payment
6. Medicines pricing methodology

RESULTS AND DISCUSSION
Italy (Tables 1 and 2)
The cost of medicines are a major component of the cost of public health.[12,18,19,20,21]

To counteract the continuous growth of drug costs, the State takes regulatory measures in 2002 for capping of the level for those costs in the amount of 13% on health in general (Law № 326/2003), which limits act to both national and regional levels. This "ceiling" was subsequently amended in 2009 to 13.3% (Legislative Decree No. 78/2009), and in this framework does not include the cost of drugs consumed by hospitals.

In 2012, again reducing the budget for the drugs used in outpatient care (Law № 135/2012) - from 13.3% to 13.1% in 2012 and in 2013. - 11.4% of total health expenditure. At the same time in 2013 the cost of medicines in hospitals has been allowed to increase by 2.4% to 3.5%. From 2013 regional structures and industry will cover in a ratio of 50%: 50% of any excess costs (above the ceiling) for drugs used in medical institutions.

In 2011, total drug costs have reached € 26.3 billion with a share of 75% reimbursed by the SSN (AIFA, 2011). Pharmaceutical expenditure per capita (including SSN-reimbursed
medicines obtained from public and private pharmacies with and without extra charge to the patient) as a whole grew by 2.5% in 2001-2010, in the southern regions of the country have higher levels costs than the national average, equivalent to € 215 per capita.

In Italy the general conditions of the system for the reimbursement of medicines are set at national level and implemented regionally such by public authorities. When authorization is granted by the European Medicines Agency (EMA) or the Italian Medicines Agency -AIFA (Agenzia Italiana del Farmaco), holders of OCs (marketing authorization) can apply for reimbursement of medicines from PFN (Prontuario Farmaceutico Nazionale).

Medicinal products are assigned to three groups – class “A”, „H” or „C”.
- Class "A" includes essential products and those intended for chronic diseases and are fully reimbursed by the health fund;
- Class "H" includes products that are fully reimbursed and are only for use in hospitals;
- Class "C” includes products which do not possess the characteristics of the class A or H and are not reimbursed.

There is another recently introduced possibility of classification of innovative products (in descending order of importance), the drugs are classified in three groups according to the severity of the diseases
I. Drugs for the treatment of “serious diseases” – those, which are with high mortality, require hospitalization or treatment of diseases with danger to the life or disability (eg neoplastic disease, Parkinson's disease, AIDS);
II. Treatments that reduce or eliminate the risk of serious illness (eg. Hypertension, obesity and osteoporosis);
III. Drugs for the treatment of “acute illnesses” (eg.: allergic rhinitis).

For each of these three classes are investigated the levels of innovation, taking into account:
- The availability of existing products;
- The level of therapeutic benefits.

The results are then determined by the presence of pre-existing treatments
A. Medicine for treatment of diseases without adequate treatment to the time of evaluation of the new product (this case concerns orphan drugs for the treatment of rare diseases), or
targeted to subgroups of patients with absolute contraindications to the use of drugs that are already on the market and for which new drugs are the only treatment option;

B. Medicines intended for the treatment of diseases in which subsets of patients are refractory or not complying to the first-line therapy (the case of anti-HIV drugs and certain anti-cancer drugs);

C. Medicines for the treatment of diseases where there is already recognized treatments.

In the case of “C” group, the product refers to one of the 3 sub-groups:

• C1. Products that offer better safety and efficacy or better pharmacokinetic profile.
• C2. Products that are pharmacological innovation, new method of operation, but not improvement over other existing therapies.
• C3. Products, which offering technological innovation, but not therapeutic advantage over existing products.

After the extent of the therapeutic effect of the new drug is reported, AIFA considered basic and “surrogate” clinical end points, and uses three classifications

A. Key benefits: reducing mortality and morbidity;

C. Partial benefits in the treatment of a disease or not there is sufficient evidence for a serious advantage (inconclusive results);

C. Small or temporary benefits for some aspects of the disease, such as partially alleviate the symptoms of serious illness.

The results of these scales are combined to determine whether a particular product is an important, moderate or little therapeutic innovation. It can put an additional limitation known as "observation AIFA".

If the manufacturer wants the product to be reimbursed the price of the drug will be determined by agreement between the manufacturer and the Committee on pricing and reimbursement CPR (Comitato Prezzi di Rimbors). The criteria used during negotiations

- Cost-effectiveness of pharmaceutical products where there is no effective therapy;
- Risk-benefit ratio compared with alternative drugs for this indication;
- The cost of daily treatment compared to products with the same efficiency;
- Assessment of the economic impact on the national health insurance system;
- Market share, which would have taken a new product;
- Prices and consumption data in European countries.
The prices of the products included in category “C” are not reimbursed from the SSN, but might be covered by additional funds.

Although the Italian health system is decentralized, pricing and reimbursement basically decided at national level and published in the Official Gazette (Gazetta officale). Regions, however, may decide to pay the patient, resulting in a price difference of medicines in different regions. AIFA recommended HTA for innovative medicines.

**France (Tables 1 and 2)**

The French population is among the biggest consumers of pharmaceutical products.[12, 22] The price of medicines, as well as in most OECD countries is determined administratively for all drugs, but the large volume of the market makes the country the third largest market for drugs, representing 6% of the annual cost of medicines in the world (after 45% for USA and 9% for Japan).

Decisions of reimbursement of medicines follow stricter national rules. The drug should be included in the "positive list" created by Ministerial Order on the advice of the Transparency Commission (CT) and the Committee on pricing (CEPS), on the basis of assurances from the manufacturers therapeutic benefit scheme (SMR). Then CT estimated SMR according to five criteria

- effectiveness of the drug and possible side effects;
- participation in the therapeutic process, available alternative therapies;
- the severity of the condition in question for which treatment is intended the drug;
- therapeutic, prophylactic or symptomatic properties of the drug;
- its importance in terms of public health.

If the SMR for a product is a "great or substantial", "moderate" or "low," but still enters in the criteria for reimbursement, the product may be included in the positive list. If the SMR is determined with low or insignificant therapeutic benefit, the drugs are not covered by the system of reimbursement from the state and public funds (SHI).

The majority of the drugs are reimbursed 65%. CT has the mandate to reassess all medicines in accordance with the new criteria for therapeutic benefit. In practice, introduced rules for medicines evaluation from 1999 led to a decrease in their prices and the rate of reimbursement - an average of 65% to 35%.
Since the establishment in 2010 of a rate of 15% coverage for drugs of low SMR, reimbursement of 171 drugs was reduced from 35% to 15%.

The regulatory authorities in France evaluated the additional therapeutic benefit of drugs compared with available similar treatments (ASMR) or to the drugs that are now available for the same pathologies.

**The price of medicines in France should be determined by**

1. ASMR—additional therapeutic benefit compared with similar available treatments;
2. The price of other drugs with the same therapeutic indications;
3. The estimated volume of sales.

Drugs with assessment ASMR 1 can get a price higher than the reference, while those with ASMR 5 will receive a price that would be reimbursed only if the price is lower than that of its alternatives.

**There are two exceptions to these rules**

1. If the volume of sales, particularly of prescription drugs is expected to be large, CEPS may request from the producers to sign price volume agreement or to make concessions to the price of reimbursed medicines;

2. CEPS may set a common price for a whole class of similar drugs when the class includes a generic substitute, which, however, is rarely prescribed.

**It should be mentioned that from 2004, drugs, used in hospital therapy may be included in two additional lists**

- Hospital medicines delivered to outpatients ("List of retrocession");
- Expensive medicines, which are paid by the health insurance system and in addition from the hospital charges for the stay of the patient on the basis of tariffs through the system of Diagnosis Related Groups (DRGs - "List with T2A").[22,23]

Promoting the prescribing and use of generic drugs due to the relatively low cost of these drugs in France (Lemorton 2008). In June 2008, the Ministry of Health decided to encourage price competition in the pharmaceutical market, allowing pharmacies to allocate 216 non-prescribing drugs that are directly accessible to the patient (still lacks analysis and data on the effect of this measure).
Overall, despite the reforms implemented by the end of 1990, the growth of drug costs remains high and stable. On the one hand the Government is facing severe compromise between two conflicting goals - to keep health care costs and to support the national pharmaceutical industry. On the other hand, doctors are reluctant to change their models of prescription of drugs. Reforms, aimed at pharmacists, are reported more success in lowering direct drug costs.

United Kingdom (Tables 1 and 2)
In the United Kingdom (UK) healthcare system is basically public, 80% of the funding comes from taxes, 12% from national insurance 4% of the fees and sundry, 3% interest income and 1% capital receipts (European observatory health Systems 2002).[24,25] Although Britain has a relatively low private insurance coverage, compared with countries like the USA, private health care is playing an increasingly larger role in terms of financing and delivering of health care services.

In the United Kingdom, which consists of England, Scotland, Wales and Northern Ireland, the decision on reimbursement of medicines is formed based on the Health Technology Assessment - HTA. Each of these countries has its own approach to HTA - in Scottish Medicines Consortium, National Institute for Health and Clinical Excellence (NICE), and the National Coordinating Centre for Health Technology Assessment (NCCHTA), Major national HTA organizations in England, Wales and Northern Ireland. NICE conduct assessments and develop guidelines and NCCHTA manage and develop the program NHS - HTA.

The primary health technology assessment conducted by NICE, could be defined in two ways
1. Evaluation of multiple technologies (Multiple Technology Appraisal);
2. Evaluation of a single technology (single data technology appraisal) (SDTA).

Both processes - MTA and SDTA - evaluate evidence of the health impact, cost and effectiveness of these health technologies, as NICE published on the site specific guidance on what to include assessments, as thus it has a clear predictability of the expectations of all stakeholders, including manufacturers and owners of authorization for use.
With regard to reimbursement and control of drug prices in the United Kingdom\textsuperscript{[25]} is applied different control schemes depending on the status of drugs. These are voluntary agreements between pharmaceutical companies and the NHS, although there are "spare" legal powers to control the prices of medicines and profit levels when a company does not propose a voluntary agreement on the basis of Articles 260-266 of the Law NHS since 2006.

With few exceptions, companies can not increase the price of any medicine without Ministry of Health has given prior approval and such does not occur if the estimated profit for the current and next financial years, respectively, over 40 % of the set in the preliminary agreements for capital investment.

Another way to control of costs is introduced in 2010, generic substitution - from primary care pharmacists who can replace the original product prescribed by the doctor with cheaper generic substitute. From 2009 came into force two new provisions relating to the pricing of medicines

1. Flexible pricing - pharmaceutical companies can increase or reduce its original list price only once to a maximum of 30% due to new evidence of therapeutic benefit or for products released after 02 September, 2007.
2. Patients access schemes. They allow the companies to offer a schemes-agreements based on improved cost-effectiveness of drugs.

And in the UK there are parallel imports of medicines, which amounts to more than 14% of sales in 2005 and cost the industry about £ 1.3 billion (according to data of the Association of the British Pharmaceutical Industry, 2006).

\textit{Germany (Tables 1 and 2)}

Regulation of drug prices in Germany differs between sectors of outpatient and inpatient care.\textsuperscript{[26,27]} While hospitals can negotiate prices with wholesalers or manufacturers, the outpatient market is undergoing much more stringent regulation. In both sectors, however basic (from producer) prices are primarily determined by pharmaceutical companies, and regulation is on the level of reporting and determining of the legal minimum sale of parallel imports. The main tools that implement health funds in Germany to control prices and reduce the cost of reimbursed medicines are

1. Discounts, rebates and price freezes;
2. The reference prices;
(3) Reimbursement within certain limits (Höchstbeträge);
(4) Reimbursement (Erstattungsbeträge);
(5) Indirect instruments such as generic substitution and parallel imports.

**In Germany the term "discount" refers to several instruments**

(1) imposed a legal concession that all pharmacies should be made to the health insurance funds for each package sold (§ 130). In 2012, rebates from pharmacies by drug prices to the health funds in the amount of € 1,20 billion, or about 4% of the cost of medicinal products paid for public funds (Bundesministerium für Gesundheit, 2013b ; Schaufler and others, 2013).

(2) extra legally regulated discount that manufacturers are obliged to make to the health insurance funds (§ 130a, Sections 1-3 and 3b). For drugs that are not included in the scheme of the reference price, the discount is 16% from August 2010 until the end of 2013. From April 2014 the discount from drug manufacturers outside the scheme of reference pricing is set at 7% patented drugs and 6% for those without a patent, but subject to reference pricing.

(3) "discounts for disease" - are made by the producers to the funds in the case of negotiated contracts to further reduce the cost of reimbursed medicinal product (§ 130a, paragraph 8).

The determination of the reference price for reimbursed medicines is another way to control the costs of drugs. This case sets a price cap for reimbursement by the health insurance funds (under § 35 of the Act), as reference prices are fixed for the same drugs, similar or comparable efficacy. It should be noted, however, that very few drugs exceed the reference price, a fact attributable to both the competition within the reference-price groups and the legal obligation for doctors to inform patients, that certain drugs should pay extra. Since 2006. pharmaceutical products, which are priced at least 30% lower than the reference price are exempt from charge. Attempts of patients to circumvent of additional payments increased demand for pharmaceutical products under the ceiling of the reference price.

As innovative medicines, the Federal Joint Committee is decided whether the new drug has additional therapeutic benefits and what are these. Drugs for which no such evidences are subject to reference pricing. If there are no other drugs with similar or the same efficiency, manufacturers should sign agreements that the price of the product must not lead to higher costs compared to the comparable therapy (pharmaceutical products with additional benefits).
By the end of 2013 reimbursement were applicable for 41 pharmaceutical products with proven additional therapeutic benefit. The parties have mutually agreed on the amount of reimbursement of 37 pharmaceutical products, the Court of Arbitration ruled for the remaining four (GKV-Spitzenverband, 2014).

Another form of indirect price regulation of the pharmaceutical market paid and reimbursed by health insurance funds requires the provision introduced in 2002 by Law to limit (ArzneimittelausgabenBegrenzungsgesetz) the cost of medicines. Law imposes an obligation to the pharmacies to sell generic drugs cheaper than the original product, provided that the doctor in the recipe indicates only the name of the active substance or has not ruled replacement with another product with the same active ingredient.

Providing a "bonus-malus" is introduced as an indirect instrument to regulate the prices of medicines in Germany in 2007 by the Act to improve the efficiency of pharmaceutical care. For some therapies it determines the average cost of Define daily dose (DDD). If the doctor who issued the prescription exceeds the average cost by more than 10%, he / she must pay a compensatory amount (malus) of the Health Insurance Fund. Conversely, doctors, comply with amendments to the law, leading to lower costs for drugs reimbursed by the health funds, receive additional bonuses paid by health funds.

Imposition of restrictive spending limits for reimbursed medicines defined as "budgets" is a measure to limit pharmaceutical expenditure in the period from 1993 to 2001. After 2002, "the expenditure ceilings" were removed and replaced with determined by negotiation prices of medicines, but they lead to a real reduction in pharmaceutical expenditure amounting to € 13.7 billion in 1992. In the period 1993-2002, the measure is effective for reducing the cost of reimbursed medicines in short and long term (Schreyögg & Busse, 2005; Busse & Riesberg, 2004). Determine and a level and for over prescribing of drugs to 125% for individual practices. Those doctors who exceed this norm must justify the hype prescription, if their arguments are not accepted, they pay the difference up to 115% of normal. The use of OTC drugs at the expense of health insurance payments reduced from 426 million prescriptions in 1992 to 72 million prescriptions in 2004, and the turnover - from € 4.4 billion to € 0.7. The sudden decline of 64% in the recipes of 2003 (197 million prescriptions) to 2004 (72 million prescriptions) and 67% in turnover to € 705 million, is a result of the modernization of the regulatory framework.[26,27,28]
Table 1. Measures of reimbursement policies in Italy, France, UK and Germany

<table>
<thead>
<tr>
<th>State</th>
<th>PLD (positive list of drugs)</th>
<th>NLD (negative list of drugs)</th>
<th>HTA</th>
<th>sharing schemes of risk</th>
<th>Copayment from patient</th>
<th>reference pricing</th>
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</thead>
<tbody>
<tr>
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<td>Yes</td>
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<td>type of pharmacoconomic evaluation</td>
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<tr>
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<tr>
<td>UK</td>
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<td>yes</td>
<td>Yes</td>
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</tr>
<tr>
<td>Germany</td>
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<td>yes</td>
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</table>

Table 2. Population and GDP of the analyzed countries

<table>
<thead>
<tr>
<th>State</th>
<th>Population (n)</th>
<th>GDP per capita (Euro)</th>
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</thead>
<tbody>
<tr>
<td>Italy</td>
<td>60 429 675</td>
<td>25300</td>
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<tr>
<td>France</td>
<td>66 864 163</td>
<td>31100</td>
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<tr>
<td>UK</td>
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<td>30200</td>
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<tr>
<td>Germany</td>
<td>79 833 625</td>
<td>33100</td>
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</table>

* Data on population are to 2015

DISCUSSION AND CONCLUSION

If the investments in health (generally speaking) are considered the investment of human and financial resources in order to achieve a high health status of the community, it is obvious that this society should monitor the cost-effectiveness of monetary or value of this investment. Therefore, the question is whether worth to spending public funds to cover the cost of a specific drug, i.e. more effective has it been?

Apparently, the decision must be taken by third parties - payers (social and health institutions or national health services or bodies that represent them), taking into account the return on investment for the pharmaceutical company, transparent prices and value for money. These decisions are political and are associated with the allocation of health spending.

Measures of detention of the costs of drugs in the system of reimbursement and in the 5 countries include positive drug list and a negative one, type of economic evaluation is also used in the five countries as well as schemes for sharing the risk, surcharge of patient and reference pricing.

There are used more and more standardized methods for systematic assessment and evaluation of criteria such as the relative effectiveness, profitability, budget impact, medical / therapeutic needs, social and ethical considerations also play a role in these decisions.
LITERATURE
1. NSI. http://www.nsi.bg/bg/content/11472/%D1%80%D0%B5%D0%B0%B0%D0%BB%D0%B5%D0%BD-%D0%B1%D0%B2%D0%BF-%D0%BD%D0%B0-%D1%87%D0%BE%D0%B2%D0%B5%D0%BA-%D0%BE%D1%82-%D0%BD%D0%B0%D1%81%D0%B5%D0%BB%D0%B5%D0%BD%D0%B8%D0%B5%D1%82%D0%BE-%D0%B8-%D1%82%D0%B5%D0%BC%D0%BD-%D0%BF%D1%80%D0%B0%D1%81%D1%82

9. Cuervo H. et al., Hospital management, S., 2000
12. A.Zlatareva, Financing pharmacotherapy of rare diseases, Sofia, 2014


20. Francesca Ferré at all., Health Systems in Transition, Vol. 16 No. 4 2014, Italy Health system review,, http://www.euro.who.int/__data/assets/pdf_file/0003/263253/HiT-Italy.pdf?ua=1

21. ISPOR, Global Health Technology Assessment Road Maps, Italy - pharmaceuticalshttp://www.ispor.org/htaroadmaps/italy.asp#2


