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Final Report with Recommendations for Reforming Bulgaria's Pharmaceutical Sector

May 2015

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List of abbreviations

ABPhM	Association of Bulgarian Pharmaceutical Manufacturers
AMI	Acute myocardial infarction
ARPharM	Association of Research-based Pharmaceutical Manufacturers in Bulgaria
ATC	Anatomical, therapeutic, chemical classification
BBP	Basic benefits package
BDA	Bulgarian Drug Agency
BGN	Bulgarian Lev
BMA	Bulgarian Medical Association
CCPs	Clinical Care Pathways
CEA	Cost-Effectiveness Analysis
CMA	Cost-Minimization Analysis
CNS	Central Nervous System
COM	Council of Ministers
CUA	Cost-Utility Analysis
DALYs	Disability-adjusted life years
DDD	Defined Daily Dose
DTCA	Direct to Consumer Advertising
EFP	Ex-Factory Price
EMA	European Medicines Agency
EMR	Electronic Medical Record
EPO	European Patent Office
ERP	External Reference Pricing
ESA	Erythropoiesis Stimulating Agent
EU	European Union
GDP	Gross Domestic Product
GNI	Gross National Income
GPs	General Practitioners
HIA	Health Insurance Act
HTA	Health Technology Assessment
ICER	Incremental Cost Effectiveness Ratio
INN	International Non-Proprietary Name
LYG	Life Years Gained
MOF	Ministry of Finance
MOH	Ministry of Health
MPHMA	Medicinal Products in Human Medicine Act
NCD	Non-Communicable Disease
NFC	National Framework Contract

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NHIF	National Health Insurance Fund
NHS	National Health Service (UK)
NICE	National Institute for Health & Care Excellence (UK)
NME	New Molecular Entity
NSI	National Statistical Institute
OECD	Organization for Economic Co-operation and Development
OOP	Out of Pocket Expenditure
OTC	Over the counter products
OTC	Over-the-Counter
PDL	Positive Drug List
POM	Prescription Only Medicine
PPP	Purchasing Power Parity
QALY	Quality Adjusted Life-Year
QoL	Quality of Life
R&D	Research and Development
RA	Rheumatoid Arthritis
RAS	Reimbursable Advisory Services
RCT	Randomized Controlled Trial
ROI	Return on Investment
RSA	Risk Sharing Arrangement
TRP	Therapeutic Reference Pricing
VAT	Value Added Tax
VBP	Value Based Pricing
WHO	World Health Organization
WTP	Willingness-to-pay
YLLs	Years of life lost
YOY	Year on year

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Executive summary and recommendations

This report presents a review of current issues in the pharmaceutical sector in Bulgaria, examining drug policy, regulation, pricing, formulary selection, distribution, expenditure, and to the extent possible, patterns of use in Bulgaria. Its recommendations are intended to serve as options for reform, by articulating short and long term strategies for managing pharmaceutical expenditure, improving system sustainability, and driving value for money in Bulgaria, thereby improving efficiency, equity, affordability and ultimately, access to prescription medicines.

Although small, the Bulgarian pharmaceutical market is showing strong growth. Medicines comprise not only a disproportionate share of health care expenditure (38% of total health expenditure, compared with an EU average of around 25%), the burden of out of pocket (OOP) costs is also excessive, possibly as high as 81% of total pharmaceutical expenditure. Of perhaps greatest concern is that rapid expenditure growth is taking place without obvious improvements in health outcomes, and at the expense of population equity.

Bulgaria does not yet have an integrated national medicines policy, and the pharmaceutical sector is characterized by various highly prescriptive and at times, arguably inconsistent policy levers. While the regulatory framework has been largely brought into line with current EU standards, existing mechanisms for listing, pricing and subsidizing medicines are not ensuring adequate value for money for the National Health Insurance Fund (NHIF), and are contributing to inefficiencies in the health sector. Current pharmaceutical policy settings appear focused on limiting NHIF outlays rather than prioritizing access and affordability, and afford little financial protection to patients.

At present the principal price-setting mechanism for medicines is international (external) reference pricing, with prices set at the level of the lowest of ten primary and seven secondary EU member states. However, sole reliance on reference pricing may not be ensuring value for money for a number of reasons—the referenced prices are 'official' prices and may not capture confidential discounts and negotiated rebates, and they may not reflect (and may not have been assessed for) value for money in the referenced member states. Moreover, they may be subject to strict controls on utilization to offset the budget impact of high unit prices in source countries, and this is unlikely to be taken into account in a simple pricing look-up. Finally the references prices are drawn from EU member states that all enjoy substantially higher per capita GDP than Bulgaria, so even if the price of a drug were shown to reflect reasonable value for money in the source country, this cannot be assumed to be the case in Bulgaria.

For some single source, and in many cases, high unit cost medicines, prices are as high, and at times even higher in absolute terms than in countries of much greater national wealth (a proxy for capacity to pay). Moreover, existing processes for listing medicines on the Positive Drug List are insufficiently influenced by considerations of cost effectiveness, and there are no explicit links between circumstances of listing and existing prescribing protocols. There are as yet no officially endorsed pharmaco-therapeutic guidelines despite at least three pieces of legislation containing provisions stipulating their development and deployment in clinical practice in Bulgaria. The net result is that utilization of several very high cost and potentially non cost-effective medicines is growing very rapidly. Currently a number of clinical guidelines are being developed, but as they do not take into account issues of cost or cost effectiveness in directing treatment, even with good adherence they may not be effective in moderating expenditure and may even increase it by promoting the uptake of new but not necessarily cost-effective therapies.

The setting of a benchmark price for multi-source medicines in the absence of any mechanisms that favor dispensing of the benchmark product or of any restrictions on the number of brands of the medicine listed on the Positive Drug List (PDL) discourages competition within the off-patent medicines market. To the extent competition exists, it is focused on discounting in the supply chain, which suggests scope for lowering prices and clawing back some of the savings currently accruing to pharmacies. Adjusting approaches to listing, pricing and procurement of multi-source medicines to create greater competition has the potential to deliver substantial savings.

The apparent focus on cost-containment, reflecting the need to control public expenditure given the above issues, contributes to the very high out-of-pocket expenses for patients. For multi-source products containing the same International Non-proprietary Name (INN) in the same pharmaceutical form, the amount of NHIF reimbursement is set as a proportion of the product with the lowest cost per Defined Daily Dose (DDD). Therapeutic reference pricing is also applied across different molecules within the same therapeutic class (where the products are considered to be of similar

efficacy and safety in a particular indication). Since actual prices often substantially exceed benchmark prices, and as levels of reimbursement by the NHIF are set as a proportion of the benchmark, OOP costs to patients can be extremely high, often substantially exceeding the NHIF contribution.

Other pharmaceutical sector policies also appear to be contributing to high OOP costs for patients and are regressive. As retail margins are proportional to drug prices, pharmacists have powerful incentives to stock and dispense more expensive products. [No explicit dispensing fees are paid by NHIF though pharmacies receive 2 BGN per prescription for prescriptions for fully subsidized items.] In addition the imposition of the full VAT rate of 20% adds to the cost burden for both the NHIF and patients. Currently OOP costs are likely to be undermining access and adherence to treatment for medicines that are important for delaying or preventing progression of non-communicable diseases, particularly cardiovascular and chronic respiratory diseases. Many drugs for chronic conditions, for which adherence to treatment is important to prevent long-term sequelae or disease progression, carry both substantial levels of co-insurance and 'premiums' over and above the NHIF's benchmark prices.

Most prescribing is by brand, both in hospitals and in ambulatory care, and substitution at pharmacy is not permitted for NHIF-subsidized prescriptions. As a result many prescriptions are written and dispensed for brands that are more expensive than the reference or benchmark price, which increases OOP costs for patients, often by substantially more than the co-insurance amount. Moreover, there are no safety nets or "stop-loss" provisions to protect individuals from catastrophic OOP costs. Consideration should be given both to mandating prescribing by international non-proprietary name (INN), and giving pharmacists the right to substitute a generic medicine for an originator brand at the point of dispensing. Where a prescription is written for a medicine that is subject to generic competition, patients should have the right to receive, and when requested, pharmacists should be required to dispense a benchmark-priced product attracting the minimum co-insurance amount - or if unable to do so, to absorb the difference in cost.

In summary, current listing and pricing mechanisms provide little or no assurance of value for money for new medicines included in the Positive Drug List and some prices for both patented and off-patent medicines compare unfavorably with countries with far greater capacity to pay. Several high cost medicines that are contributing significantly to rapid expenditure growth are unlikely to be cost effective in Bulgaria and should be subject to price (re)negotiation, explicit restrictions on use, and in some cases, even disinvestment (delisting). If Bulgaria were also able to encourage greater competition in the off-patent medicines market, this, together with measures to address demand and promote rational prescribing and generic uptake, could significantly improve efficiency in current pharmaceutical expenditure. Reconfiguring the role and remit, structure and procedures of the National Council on Prices and Reimbursement of Medicinal Products (the Pricing Council) is critical to improving efficiency and ensuring value for money.

To that end, in the short term, results of HTAs conducted in other jurisdictions could be adapted to inform current and future decisions on listing and pricing in Bulgaria. While the results of an economic evaluation in one jurisdiction or setting may not be directly applicable in another setting, some HTA data will be relevant across different settings and contexts, such as evidence from randomized controlled trials regarding the comparative efficacy and effectiveness of interventions. Factors such as burden of disease, patterns of clinical practice, unit costs and patterns of resource utilization, availability of healthcare resources and budget constraints, as well as the choice of appropriate comparator are more country-specific, and country-specific evaluations which reflect the needs of decision-makers within country are ultimately to be preferred.[1] Nevertheless if a high-income country finds that a particular health technology is not cost-effective at a given price, it is highly unlikely to be cost-effective at that price in a low- and middle-income setting.[2] Thus applying what is effectively a 'de facto' HTA (see Box 1)—that is, referencing prices and conditions of listing in another jurisdiction with established HTA processes, and determining a notional 'cost-effective price' by adjusting for relative PPP-adjusted per capita GDP—could be used in the short term to *guide* listing decisions and to *inform* price negotiations.

1 WHO/HAI Project on Medicine Prices and Availability. Review Series on Pharmaceutical Pricing Policies and Interventions. *Working Paper 6: The Role of Health Technology in Medicine Pricing and Reimbursement*. WHO, June 2013

2 Moran V. Health technology assessment in Europe: Communicating and applying lessons learned from high-income countries to middle-income countries. *Journal of Management & Marketing in Healthcare*, 2010, 3(2):141-149.

To operationalize this in Bulgaria the NHIF could begin by simply adapting the results of HTA analyses from the UK, (or Belgium, France or any other country with robust HTA processes), and use these to modify conditions of listing and inform (re)negotiation of prices of existing medicines. Renegotiating the prices of just four drugs in Annex II – nilotinib, rituximab, pazopanib and pemetrexed – to approximate UK prices could potentially reduce spending by around BGN 10.8 milllion, based on 2014 NHIF expenditure. However, applying the de facto HTA method to drugs in Annex II, and reducing the prices of just 4 of the top 5 medicines (by NHIF expenditure) to prices approximating a similar degree of cost effectiveness to those in the UK, could generate savings of up to BGN 21 million.[3] While obtaining price reductions of that magnitude through negotiation would clearly be exceptionally challenging (and given the extensive use of reference pricing within the EU might need to be obtained by way of confidential discounts or rebates), the calculation nevertheless highlights the true opportunity costs of the current prices and supports the need for realistic assessment of value for money of medicines proposed for the PDL.

Box 1: What is '*de facto*' health technology assessment (HTA)?

The term '*de facto*' HTA is used to refer to a method of assessing whether a healthcare technology represents value for money in one setting, by utilizing or transferring the results of an HTA performed in another. Its application requires the selection of a reference country from which details of prices, HTA processes and outcomes are known, and assumes a fixed relationship between cost-effectiveness and (PPP-adjusted) per capita GDP *(a proxy for capacity to pay)*.

$$\text{'Cost Effective' Price (Country A)} = \text{'Cost Effective' Price (Country B)} \times \frac{\text{(PPP-adjusted) per capita GDP (Country A)}}{\text{(PPP-adjusted) per capita GDP (Country B)}}$$

A drug is unlikely to be cost effective in Country A at a price higher than the price in the reference country adjusted by the ratio of the Country A's (PPP-adjusted) per capita GDP to Country B's (PPP- adjusted) per capita GDP.

While this approach does not capture the influence of local factors that may affect the cost effectiveness and budget impact of a new therapy, it is a useful technique for informing price negotiations in the absence of local, evidence-based considerations of value for money.

For drugs under consideration for inclusion in the PDL, applying this method would mean setting conditions of listing that are consistent with those in a jurisdiction where the drug has been subject to rigorous HTA, and declining to list drugs for indications not considered cost-effective or clinically appropriate there. Prices higher than those in the reference jurisdiction after adjustment for relative per capita GDP would represent the *upper limit of cost effectiveness for these medicines*. This process could be introduced quite quickly, and should be possible to implement within existing resources.

In the short term savings should be achievable through the introduction of more competitive procurement mechanisms for multi- and some single source medicines, supported by other measures described above. This could be complemented by utilizing a de facto HTA approach to the listing and pricing of other single source and high cost medicines in the short term, while in the medium term working towards the gradual development of HTA processes and capacity.

In addition, consideration could be given to the introduction of risk sharing arrangements (RSAs) to assist both in moderating and improving predictability of overall expenditure. For example, price-volume agreements or expenditure caps could be a condition of inclusion in the PDL for drugs for which utilization and budget impact are uncertain, or for which prescribing is likely to be difficult to control. Listing and pricing of certain high cost drugs could be made contingent on the proportion of patients achieving a specified response to treatment, with rebates where outcomes anticipated from clinical trial data (and on which estimates of cost effectiveness are predicated) are not reflected in practice. RSAs do however require skills in developing estimates and in assessing the evidence to distinguish high value from low

3 Based on GDP per capita, PPP (current international $) UK $38,451.7, Bulgaria $15,731.70. At http://data.worldbank.org/indicator/NY.GDP.PCAP.PP.CD

value use. For performance-based contracts patient registries or other mechanisms for recording and aggregating patient outcomes may also be required.

Over time however, the development and introduction of robust, evidence-based HTA processes within Bulgaria will be important to improve the country's capacity to a) assess value for money in the selection, listing and pricing of medicines and b) provide a means of prioritizing expenditure in a resource limited environment. The development of a critical mass of practitioners with adequate expertise in HTA methods will take some time and would need to be appropriately sequenced. One approach could be to utilize a "train the trainer" model to develop a core of intensively-trained individuals, and by ensuring that they are able to network effectively with relevant individuals and organizations both within and outside Bulgaria, domestic capacity could be developed within a few years. The necessary expertise need not reside solely within the Pricing Council or the MoH, though some capacity should clearly be developed and retained there, together with the necessary administrative supports. A more practical model may be to have trained professionals distributed across several academic and quasi-academic settings, as well as within Government. This would facilitate expansion of the skill base.

In the short-term (12-24 months) consideration should be given to mandating comparative cost effectiveness as a key criterion for addition to the PDL. To operationalize this, one option would be to introduce an interim *de facto* HTA process, accompanied by a review and recalibration of subsidized indications, particularly for high cost Annex 2 drugs. Direct price negotiations for those drugs identified as unlikely to be cost effective at current prices should be considered, and these could be informed by the de facto HTA method to determine target prices. At the same time HTA capacity-building could commence through focused technical training, and gap analyses initiated to identify information and data needed to inform future decision-making

In the medium term (2-4 years) processes, guidelines, methods and decision criteria for a robust and rigorous HTA framework could be developed to support listing/delisting of medicines. One approach might be to partner with one or more academic institutions, some of which may have existing expertise, to continue the process[4] of developing (or adapting other countries') guidelines for the submission and evaluation of the required evidence. HTA capacity could be gradually expanded through ongoing training and professional development activities. Mandatory HTA as prerequisite for listing/delisting of medicines could then be introduced by law to replace the interim de facto process once guidelines and methods are agreed and promulgated.

In the longer term (5+ years) rigorous processes should ideally be established to review and update national drug formularies. The role of HTA as a prerequisite for the listing/delisting of medicines could gradually be consolidated and its application considered for non-drug technologies, products and services as appropriate.

During the drafting of this report, the Ministry of Health released a document entitled *Concept Note: Health 2020 Goals*[5] which, *inter alia*, emphasizes the importance of increasing the efficiency of drug treatment, of building capacity for the evaluation of health technologies, of the role of clinical guidelines and treatment algorithms, and of prescribing and use of medicines that are effective and cost-effective. Importantly it also noted that

> *control over health expenditures must be governed by the understanding that it is essentially a method for their optimization for the achievement of particular health outcomes, instead of an end in itself to decrease and limit them.*

The findings and recommendations of this report are consistent with those sentiments.

4 The development of draft submission guidelines is already underway within the Pricing Council

5 At http://www.mh.government.bg/Articles.aspx?lang=bgBG&pageid=472&home=true&categoryid=7573

Table 1: Summary of Recommendations

Goal	Policy options recommended for consideration
1. Greater clarity in policy objectives	Development of an integrated national medicines policy through focused stakeholder engagement.
2. More effective formulary decision making and pricing processes	Reconfigure the role, remit, structure, composition and methods of operation of the National Council on Pricing and Reimbursement of Medicines. Improve professional capacity in economic evaluation and introduce comparative cost effectiveness as a mandatory criterion for inclusion of a drug in the PDL Establish a simplified HTA process until HTA capacity and processes are developed Modify the use of external reference pricing pending implementation of full HTA Introduce mandatory Budget Impact Assessment for new medicines Increase time available for evaluation and listing of medicines on the PDL to allow for effective HTA Introduce competitive tendering for off-patent medicines and drugs in selected therapeutic classes with limits on the number of products and suppliers permitted for inclusion in the PDL, and with enforceable supply guarantees [6] Review the current PDL and consider delisting or restricting single source products unlikely to be cost effective in Bulgaria; renegotiate prices where possible, Apply restrictions on listing to reflect the extent of cost effectiveness, and develop risk sharing arrangements (RSAs) that reflect these.
3. Improved access, equity, and affordability	Introduce provider and consumer awareness campaigns regarding a) the safety, efficacy and quality of generic medicines; b) opportunities to save money at pharmacy by choosing generics Introduce flat co-payments to improve certainty and affordability for patients Apply savings achieved through improved market competition to raising levels of reimbursement for existing, chronic therapies (as opposed to new medicines)
4. Better management of utilization and promotion of rational use	Introduce mandatory, national, consensus clinical treatment guidelines based on evidence of effectiveness *and* cost effectiveness. Facilitate understanding and awareness of these guidelines and Introduce training in "good prescribing" into the curricula of medical students across Bulgaria. Promote rational use and encourage or preferably, mandate 'INN" prescribing Introduce indicative individual prescribing budgets, with monitoring of prescribing behavior and feedback to prescribers Establish an entity to provide independent drug information and support rational prescribing Strengthen the capacity of the BDA to effectively regulate promotional activities by the pharmaceutical industry.
5. Improved distribution chain	Permit and encourage substitution at pharmacy Introduce dispensing fees and fixed retail margins Establish incentives for pharmacies to dispense benchmark-priced products Develop clawback arrangements to take advantage of discounting in the distribution chain
6. A more sustainable system	Reduce VAT to the concessional rate. Require supply guarantees to discourage parallel export Adjust prices across the board if expenditure growth exceeds GDP growth .

6 A recent legislative proposal involves the introduction of electronic tendering for public procurement of medicines.

1. Introduction and Scope of the Report

In August 2014, the Government of the Republic of Bulgaria and the World Bank ("the Bank") entered into an agreement generally referred to as the Health Financing Reimbursable Advisory Services (RAS). The objective of this RAS is to support the Government as it lays the groundwork for implementing its National Health Strategy 2014-2020.

2. Specifically, the Bank is assisting the Ministry of Health to develop, evaluate, and implement options in the area of health financing, to improve the efficiency, equity, financial protection, and long-term sustainability of the health system. Part of that task was to develop a standalone report on pharmaceutical sector issues, with actionable recommendations for improving efficiency, equity, affordability and sustainability in access to prescription medicines in Bulgaria.

3. In order to present a document that was self-contained, much of the narrative describing the current state of the pharmaceutical sector presented in the earlier Diagnostic Report has been reproduced here. This subsequent report is intended to complement that by drawing on the previous analyses to articulate reform options intended to improve efficiency, equity, affordability and long-term sustainability in access to prescription medicines for the people of Bulgaria.

4. What should be the pharmaceutical policy priorities? Even among countries that share similar policy objectives, pharmaceutical policy choices will be influenced by social values and priorities; political, legal, and historical contexts; economic and budgetary pressures; systems financing and insurance arrangements; and perceptions of equity and affordability.

5. Nevertheless, irrespective of the specific social, political, regulatory, and financial conditions that exist, there are certain common themes that have been found to be important priorities in otherwise disparate countries and settings. Broadly these may be described as:

- Leveraging market power;
- Focusing on purchasing outcomes rather than products;
- Ensuring value for money in drug selection;
- Encouraging competition in the off-patent market and promoting the use of generic medicines;
- Identifying and eliminating perverse incentives; and
- Promoting rational drug use.

6. Importantly, these themes are echoed in the Ministry of Health's *Concept Note: Health 2020 Goals*[7] released during the drafting of this report. It speaks, *inter alia*, of the importance of increasing the efficiency of drug treatment, of building capacity for the evaluation of health technologies, of the role of clinical guidelines and treatment algorithms, and of prescribing and use of medicines that are effective and cost-effective. Significantly, it also notes that

> *" … control over health expenditures must be governed by the understanding that it is essentially a method for their optimization for the achievement of particular health outcomes, instead of an end in itself to decrease and limit them."*

7 At http://www.mh.government.bg/Articles.aspx?lang=bgBG&pageid=472&home=true&categoryid=7573

2. Current Situation and Key Issues

2.1 The Bulgarian context

7. Structural inefficiencies in the current health system together coupled with demographic, epidemiological, and economic trends pose significant challenges for public financing of health services in Bulgaria. With the population both ageing and in overall decline, a substantial proportion of the population is either poor, or highly vulnerable to falling into poverty. Bulgaria's health delivery system gives insufficient priority to investment in primary care, and is poorly equipped to address the growing burden of non-communicable diseases.

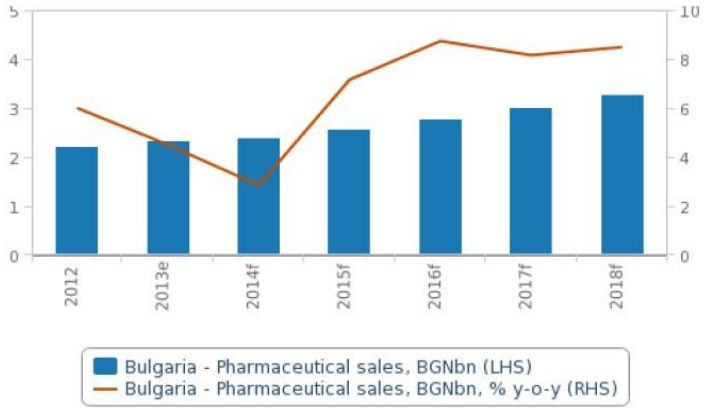
8. According to data from the National Health Accounts, in 2012 around BGN 6.3 billion was spent on health care in Bulgaria, 51 percent of which was public expenditure, largely disbursed through the NHIF. The remainder is private expenditure, mostly out of pocket (OOP) fees and charges levied at the time individuals seek care. Medicines comprise not only a disproportionate share of health care expenditure (38% of total health expenditure, compared with an EU average of around 25%), but the burden of out of pocket (OOP) costs is also excessive, accounting for possibly as much as 81% of total pharmaceutical expenditure. Of perhaps greatest concern is that rapid expenditure growth is taking place without obvious improvements in health outcomes, and at the expense of population equity.

9. Lacking a comprehensive and integrated national medicines policy, the Bulgarian pharmaceutical sector is characterized by various highly prescriptive and at times, ineffective and arguably counterproductive policy levers. While the regulatory framework has been largely brought into line with current EU standards, existing mechanisms for listing, pricing and subsidizing medicines are not ensuring adequate value for money for the NHIF, and are fueling rapid growth in expenditure. Current pharmaceutical policy settings appear to prioritize limiting NHIF outlays rather than promoting access and affordability, and offer little financial protection to patients.

2.2 The Pharmaceutical market

10. Although the Bulgarian pharmaceutical market is one of the EU's smallest, it has grown strongly over the past few years, and the pharmaceutical industry is one of the fastest growing sectors of the Bulgarian economy.[8] In 2011 the Bulgarian market was valued at BGN 2.1 billion, an increase of 12% over 2010, and it grew another 10.5% to a value of BGN 2.32 billion (USD 1.57 billion) from 2011-2013.[8] Figure 1 refers.

Figure 1: Pharmaceutical sales in Bulgaria 2012-2018



Source: Ministry of Foreign Affairs, Denmark. Pharmaceutical and Healthcare Sector, Bulgaria, 2014.

8 Ministry of Foreign Affairs, Denmark. Pharmaceutical and Healthcare Sector, Bulgaria, 2014. At http://bulgarien.um.dk/da/~/media/Bulgarien/Documents/Pharmaceutics%20and%20Healthcare_2014.pdf

11. This growth has been mainly attributed to two factors: increased NHIF expenditure on oncology and other high cost medicines, and growing consumer spending on over the counter (OTC) products. Growth in recent years is also likely to have been stimulated by the opening of the market, partly a result of harmonization of Bulgarian regulatory processes with EU regulations, which began in 1995 and was finalized in preparation for Bulgaria's EU accession in January 2007.[9]

12. Hospital consumption accounted for around 18% of the market in 2009, with another 18% being ambulatory care medicines reimbursed by the NHIF, and with OTC medicines making up nearly 17% of the total market (the rest being non-reimbursed prescription medicines).[9]

2.3 Regulatory framework

13. The accession of Bulgaria to the European Union in 2007 and its participation in the nCADREAC Agreement has facilitated the establishment of EU standards of drug regulation. The implementation of the Medicinal Products in Human Medicine Act (MPHMA)[10] has been instrumental in this. The law was drafted in 2007 to align the Bulgarian regulatory framework with European standards, but has since undergone 20 amendments. The scope of the MPHMA is broad, covering the role and responsibilities of the Bulgarian Drug Agency (BDA) as regulatory body dealing with medicinal products marketing authorizations, distribution, import, advertising etc., as well as provisions relating to the pricing of prescription and over-the-counter (OTC) medicines[11] and the establishment and maintenance of the Positive Drug List (PDL). For product registration it provides for centralized, decentralized and national procedures.

14. In addition to the MPHMA and the various amendments to it, the sector is also subject to a significant number or other laws and ordinances. Of particular relevance are:

- Health Law (1 January 2005);
- Health Facilities Law (5 July 1999);
- Ordinance on the Terms, Rules and Procedure for Regulation and Registration of Prices for Medicinal Products (30 April 2013);
- Ordinance № 4 on the terms and conditions for prescribing and dispensing of medicines (4 March 2009);
- Ordinance No 10 on the terms and conditions for payment of medicinal products, dietary foods under Art. 262, para 6, part 1 of the MPHMA as well as medicinal products for health-related activities under Art. 82, para 2, part 3 of the Health Act (24 March 2009);
- Ordinance № 28 on the structure, terms and conditions of work of the pharmacies and nomenclature of medicinal products (9 December 2008);
- Ordinance № 34 on the terms and conditions for payment from the state budget for the treatment of diseases outside the scope of mandatory health insurance (25 November 2005);
- Ordinance № 38 defining the list of diseases for which medicines, medical devices and dietary foods for outpatient treatment fully or partially paid for by the NHIF (16 November 2004);
- Ordinance № 39 on the principles and requirements of Good Distribution Practice (13 September 2007); and
- Ordinance № 40 for determining the basic package of health services guaranteed by the NHIF budget (24 November 2004),

15. The Bulgarian Drug Agency (BDA) reports to the Ministry of Health and is responsible for assessing and ensuring the quality, effectiveness and safety of medicinal products. Its role includes:

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9 Andre G et al. *Pharmaceutical Health Information System (PHIS) Pharma Profile*, Bulgaria 2010.

10 Medicinal Products in Human Medicine Act 2007. At http://en.bda.bg/images/stories/documents/legal_acts/ZLPHM_en.pdf

11 In conjunction with the *Ordinance on the Terms, Rules and Procedure for Regulation and Registration of Prices for Medicinal Products*, effective 30 April 2013

- Marketing authorization for medicines;
- Authorization and oversight of manufacturing, import, wholesaling and retailing of medicines;
- Authorization and oversight of clinical trials;
- Advertising;
- Pharmacovigilance and drug information;
- Classification (scheduling) of medicines.

16. The BDA is funded in part from the budget of the Ministry of Health as well as from revenues generated by its activities, which include fees for laboratory analyses, application and evaluation fees, annual registration charges, and GMP inspections. Fees and charges are set by the Council of Ministers.

2.4 Drug selection and pricing

Role of the Pricing Council

17. A 2011 amendment to the MPHMA replaced two separate Commissions with responsibility for pricing of medicines and management of the Positive Drug List respectively, with a single new entity, the National Council on Prices and Reimbursement of Medicinal Products (hereinafter referred to as the Pricing Council).[12]

18. The Pricing Council is a state budget-supported legal entity, with the status of a state commission based in the city of Sofia. It comprises a chair and 6 members (3 of whom must be physicians or pharmacists, 2 economists and 2 lawyers, all with experience in their specialties of not less than 5 years) and is supported by a Secretariat.[13]

19. The Pricing Council's role includes registering the maximum retail selling prices of over-the-counter medicines and makes decisions on the inclusion and pricing of medicines on the Positive Drug List (PDL), as well as setting maximum (ceiling) prices for all other medicines.[14] The price-setting mechanisms and processes are outlined in the MPHMA and set out in more detail in the 2013 *Ordinance on the Terms, Rules and Procedure for Regulation and Registration of Prices for Medicinal Products* (the Pricing Ordinance).[15]

20. The Pricing Council's role also includes approving, revoking or modifying pharmaco-therapeutic guidelines, as well as the recommendations for treatment algorithms proposed by the national consultants, various medical societies and experts. However to date no guidelines have been finalized, though several are currently in development.

21. The Pricing Council meets weekly, and direct updates to the reimbursement list (RL) fortnightly, which variously involve changes to prices, available brands, and levels of reimbursement for any of the existing medicines on the reimbursement list. Prices may also be routinely adjusted for inflation. The MPHMA also sets out timeframes for the Pricing Council's decision- making which are:

- 60 days for listing and pricing of new prescription medicines to be included in the PDL;
- 30 days for listing and pricing of generic medicines, and for setting maximum prices for prescription medicines not subject to reimbursement and over-the-counter (OTC) products, from the date of filing of the application with the Pricing Council.

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12 See http://www.ncpr.bg/en

13 See http://www.ncpr.bg/en/ncprmp/structure/organogram

14 The Pricing Council thus sets the price of all drugs marketed in Bulgaria. The positive drug list (PDL) is the more restrictive list of drugs that are (to a greater or lesser degree) subsidized with public funds. The reimbursement list is the list of outpatient medicines reimbursed by the NHIF (Annex 1)

15 *Ordinance on the Terms, Rules and Procedure for Regulation and Registration of Prices for Medicinal Products*, effective 30 April 2013. At http://www.ncpr.bg/en/regulations/bulgarian-legislation/regulations/. This supersedes Ordinance 10 of 24 March 2009 on the Terms and Conditions for Payment of Drug Products.

Pricing mechanisms

22. The primary price-setting mechanism is international (external) reference pricing. For new prescription medicines ex-factory prices are determined by considering 'official' prices in ten primary (Romania, France, Latvia, Greece, Slovakia, Lithuania, Portugal, Italy, Slovenia and Spain) and seven secondary (Belgium, the Czech Republic, Poland, Denmark, Hungary Finland and Estonia) EU member states. The Bulgarian ex-factory price is then set at the level of the *lowest* price among these jurisdictions. Links to the sources of the pricing information are provided on the Pricing Council website.[16]

23. However, international price comparisons can be significantly affected by manufacturers' marketing strategies, the relative importance of the market segment, regulatory controls, patent expiration dates, exchange rate movements, taxation policies, supply chain efficiency, use of health technology assessment or value-based pricing, and demand-side behaviours.

24. In particular, the referenced prices:

- are 'official' prices and may not capture confidential discounts and rebates;
- may not reflect (and may not have been assessed for) reasonable value for money in the referenced member states;
- may be offset with narrow indications and strict controls on utilization (submitted pricing data do not take into account indications for use).

25. All referenced member states have substantially higher per capita GDP than Bulgaria, so even if the price of a drug reflects reasonable value for money in the source country, this may not be the case in Bulgaria. At the very least the drug will be less affordable in Bulgaria.

26. Wholesale and retail margins proportional to the drug prices are set by the Ministry of Health and are regressive. Wholesale mark-ups range from 4-7%, with a maximum of BGN 10. Retail mark-ups vary from 16-20%, with a maximum of BGN 25. These are added along with 20% VAT to form the maximum retail price via a complex formula shown in

Table 2.

Table 2: Wholesale and retail markups for medicines

Ex-Factory Price				Wholesale Price					Retail Price			
Price (BGN)	VAT (BGN)	Total with VAT	Margin (%)	Margin (BGN)	Price (BGN)	VAT (BGN)	Total with VAT	Margin (%)	Margin (BGN)	Price (BGN)	VAT (BGN)	Total with VAT
5	1.00	6.00	7%	0.35	5.35	1.07	6.42	20%	1.00	6.35	1.27	7.62
10	2.00	12.00	7%	0.70	10.70	2.14	12.84	20%	2.00	12.70	2.54	15.24
30	6.00	36.00	6%	1.80	31.80	6.36	38.16	18%	5.40	37.20	7.44	44.64
50	10.00	60.00	4%	2.00	52.00	10.40	62.40	16%	8.00	60.00	12.00	72.00
100	20.00	120.00	4%	4.00	104.00	20.80	124.8	16%	16.00	120.00	24.00	144.00
200	40.00	240.00	4%	8.00	208.00	41.60	249.6	16%	25.00	233.00	46.60	279.60
500	100.00	600.00	4%	10.00	510.00	102.00	612.00	16%	25.00	535.00	107.00	642.00

16 See http://www.ncpr.bg/images/Referentni_darjavi/Tablica%20za%20saita_03.10.2014-ENGLISH.htm. The referenced prices may be ex-factory, wholesale or retail prices, with and without VAT. It is unclear how the determination is made as to which price is in fact the lowest and therefore the one referenced.

27. At 20% VAT on medicines is very high. Bulgaria is one the few EU member states that does not apply a concessional rate to medicines[17,18] although, at 9%, even the concessional rate is substantially higher than the rate applied to medicines in some countries. The UK, Ireland and Malta do not apply VAT to medicines, and in Spain, France, Croatia, Cyprus, Lithuania and Hungary the rate is 5% or less.

28. Consideration should be given to reducing the VAT rate to a level similar to other Central and Eastern European countries. In an environment in which consumers can pay significant amounts out-of-pocket for medicines, the VAT is in effect a levy on the health care budget that, like co-insurance, differentially impacts lower SES groups, thus undermining any implied equity objective. Moreover, not only do the vast bulk of OOP health costs derive from medicines, the burden falls most heavily on the poorest in Bulgaria, as shown in Table 3.

Table 3: Breakdown of out-of-pocket payments by type of care and income quintile (2013)

Quintile	Pharmaceutical products	Other medical products	Therapeutic appliances	Medical services	Dental services	Paramedical services	Hospital services	Total
Poorest	**300.6 (85%)**	0.8 (0%)	9.2 (3%)	10.9 (3%)	8.6 (2%)	3.9 (1%)	20.6 (6%)	354.6
2	**386.4 (84%)**	2.7 (1%)	16.7 (4%)	13.7 (3%)	17.2 (4%)	8.1 (2%)	17.3 (4%)	462.1
3	**437.5 (72%)**	3.8 (1%)	24.4 (4%)	21.1 (3%)	31.3 (5%)	10.3 (2%)	79.8 (13%)	608.2
4	**390.1 (73%)**	2.3 (0%)	32.7 (6%)	22.8 (4%)	43.3 (8%)	17.1 (3%)	28.3 (5%)	536.6
Richest	**452.8 (64%)**	3.4 (0%)	34.2 (5%)	40.7 (6%)	98.0 (14%)	36.2 (5%)	44.6 (6%)	709.9
Bulgaria	**393.4 (74%)**	2.6 (0%)	23.4 (4%)	21.9 (4%)	39.7 (7%)	15.1 (3%)	38.1 (7%)	534.2

Pricing of generic medicines

29. The ex-factory price of the *first* generic version of a medicine listed on the PDL may not exceed 80% of the ex-factory price of the reference product included in the PDL. Thereafter generic pricing is subject to external referencing. In other words, although a statutory price reduction is applied at the point of initial generic market entry, *there is no mechanism to drive further price reductions within the off-patent market.* For off-patent medicines more competitive pricing could create savings that could support expenditure-neutral increases in NHIF reimbursement rates, particularly for drugs used in chronic conditions for which long-term adherence is important for the prevention of long term sequelae.

30. For each multi-source medicine a notional reference or benchmark price is set at the level of the lowest cost per Defined Daily Dose (DDD) for any brand or presentation of that medicine.[19] This benchmark pricing is also applied across different molecules within the same ATC subgroup where the products are considered to be of similar efficacy and safety for a particular indication. The benchmark price within the 'cluster' of drugs is set at the level of the lowest cost/DDD for any of the drugs within that cluster. This is then the 'price' against which the level of reimbursement is set.

31. As a result of this therapeutic reference pricing there are few incentives for competition in the off-patent market. As long as the ex- factory price of a multisource medicine is not higher than 80% of that of the originator, and the price is shown to be no higher than the lowest price for the same presentation in any of the specified reference countries, the actual price can substantially exceed the current benchmark in terms of cost/ DDD, with any excess becoming an OOP cost to the patient. (See Table 4 below)

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17 European Commission. VAT Rates Applied in the Member States of the European Union, January 2015. At http://ec.europa.eu/taxation_customs/resources/documents/taxation/vat/how_vat_works/rates/vat_rates_en.pdf

18 The 9% concessional rate appears to be applied only to hotel rooms.

19 The Defined Daily Dose (DDD) is the assumed average maintenance dose per day for a drug used for its main indication in adults. *Importantly*, *the DDD is a notional metric* and does not necessarily reflect the recommended or actual prescribed dose. Moreover, *an observation that two drugs in a given class have the same DDD for a given indication does not imply that they are of equivalent efficacy*.

32. Section 264.2 of the MPHMA sets out notification requirements for suppliers of products whose prices set benchmarks, but it is not clear if suppliers are required to guarantee supply of a minimum proportion of the overall market. It is also not specified whether and how the unavailability of the benchmark-priced product triggers a (presumably upward) revision of the benchmark price. It is therefore unclear as to what, if any, mechanisms exist to ensure that benchmark-priced products are either available for supply or stocked by pharmacists and therefore available to patients.

Pricing of OTC medicines

33. Unlike most EU countries where no price controls are applied to over the counter (OTC) medicines, pricing in Bulgaria is ostensibly 'free' but is nevertheless subject to a 2013 transitional rule stating that registered maximum sales prices of OTCs could not be increased by more than the applicable inflation rate over the period since the preceding price registration. Although the rule was transitional it has since been extended to apply until the end of 2015.

The Positive Drug List

34. The Positive Drug List comprises four annexes:

- Annex I (the Reimbursement List): lists those outpatient medicines paid for by the NHIF and the level of subsidy they receive, as established by the Health Insurance Act (HIA)[20];
- Annex II: lists medicines funded from the budgets of 'medical-treatment' facilities;
- Annex III: lists medicines for the treatment of HIV/AIDS and certain communicable diseases outside the scope of the HIA, as well as vaccines for compulsory immunizations; and
- Annex IV: sets out the ceiling prices for medicines included in the PDL.

35. Chapter 6 of the Pricing Ordinance sets out the criteria for the inclusion of medicines in the PDL. To be considered for listing, the medicine must first have marketing approval in Bulgaria, as well as evidence of coverage by health insurance programs in at least five of the 10 primary reference countries**.** Evidence of coverage does not however, require or imply evidence of satisfactory health technology assessment, and thus is not an indicator of cost effectiveness. As such the requirement adds no additional value added to the assessment of the therapeutic efficiency of the medicine, apart from the other criteria used in Bulgaria, which to big extent are the same as in most of the other countries. The Bulgarian Commission on Protection of Competition (CPC) has suggested that, given other characteristics of the Bulgarian pharmaceutical market, in particular its small size, low public spending on medicines, and low reimbursement prices, this requirement may be restricting and delaying access to the national reimbursement market by originators. However the apparently rapid listing of new high cost medicines on the PDL, and a review of current prices suggest that this is unlikely to be the case.[21]

36. For new medicines, a range of clinical parameters and 'pharmacoeconomic indicators' is then evaluated, from evidence presented in the application dossier submitted by the drug's manufacturer or supplier. The 'pharmacoeconomic indicators' include the cost of therapy; a comparison of the costs of therapy with available alternatives; the cost-benefit ratio; an economic evaluation of the additional benefits offered by the therapy; and an analysis of anticipated budget impact. For each group of criteria a number of 'points' is awarded**,** with 'clinical factors' receiving a maximum of 95 points, and 'pharmacoeconomic factors' a maximum of 40 points.

37. A minimum of 60 points is required for approval, thus a product considered clinically effective may be approved even if scoring poorly on economic factors and failing to show evidence of reasonable cost effectiveness**.** The process and criteria for the assessment of the economic data are not detailed in the Ordinance. Moreover members of staff of

20 The reimbursement list in Annex 1 also includes some consumables such as glucose test strips and stoma appliances.

21 Organization for Economic Co-operation and Development. *Competition Issues In The Distribution Of Pharmaceuticals*. OECD DAF/COMP/GF/WD(2014)2, 2014.

the Pricing Council indicated that they did not have sufficient expertise in pharmacoeconomic (PE) evaluation of medicines to undertake rigorous assessments of PE data submitted by applicants.

38. The assessment is made more challenging by virtue of the short timeframes specified in the MPHMA for the Pricing Council's decision-making (60 days for listing and pricing of new prescription medicines to be included in the PDL). The rationale for this is obscure. While timely decision-making is desirable, considering the practices of other bodies undertaking similar assessments, this is unlikely to be sufficient for rigorous assessment of the clinical and economic performance of new medicines, particularly those likely to give rise to substantial budget impact, and for which new or updated treatment protocols may be needed. The *European Transparency Directive No 89/105/EEC* currently allows member states up to 90 days for pricing decisions and up to 180 days for combined pricing and reimbursement decisions.[22]

39. For the evaluation of a new medicine for inclusion on the PDL and establishment of a price under Article 261 a of MPHMA, the Pricing Council receives a fee of BGN 1,500.[23] This appears modest in relation to the effort required and the potential market available to a medicine listed on the PDL and subject to NHIF reimbursement.

40. Reasons for the Pricing Council's decisions are not made public. Few applications for inclusion of new drugs on the PDL are rejected. Any decision to refuse an application to include, change or exclude a medicine from the PDL, or endorse a proposed price is appealable to the Transparency Commission (TC). The TC is also established by the MPHMA, with members appointed by the Council of Ministers from nominations from the Minister of Health, the Ministry of Health, the Ministry of Labour and Social Policy, the Bulgarian Drug Agency, the National Health Insurance Fund, the Bulgarian Physicians' Union, the Bulgarian Dentists' Union, the Bulgarian Pharmacists' Union, and from patient and pharmaceutical industry organizations.

41. The PDL is published by the Pricing Council, and for existing drugs is updated on the 2nd and 16th day of each month. New products are only added on the 1st January each year, and the Pricing Council may only change the level of reimbursement of a medicine in PDL once a year, although price changes can occur more frequently. The ceiling price can be increased only 12 months after the last approval of the price. However if the supplier wishes to reduce the ceiling price, this can be given effect at any time.[24]

Levels of Reimbursement

42. The Pricing Ordinance also sets out the procedures for determining the amount of reimbursement of products in the Reimbursement List. These are said to be determined according to perceived clinical significance, but this appears to be applied inconsistently. All products in Annex III, as well as those in Annex I (the Reimbursement List) for chronic diseases causing 'severe disruptions in the quality or life or disablement and requiring prolonged treatment' are said to be subject to full (100%) reimbursement. Yet subsidies for oral agents for diabetes, for example, vary between 25% and 100%. Medicines for chronic diseases with widespread prevalence receive 75% subsidy; for all others reimbursement is *up to* 50%, with the actual level determined by a complex assessment of a range of factors that include whether use of the product is considered to be essential, preventive, palliative, symptomatic or for maintenance treatment; the social significance of the condition under treatment; the duration of treatment; 'accepted' treatment

22 The EU Transparency Directive No 89/105/EEC specifies a series of procedural requirements to ensure transparency of pricing and reimbursement measures adopted by the Member States. These include specific time limits for pricing and reimbursement decisions (90 days for pricing, 90 days for reimbursement or 180 days for combined pricing and reimbursement decisions). The Directive also requires competent national authorities to provide a statement of reasons based on objective and verifiable criteria for each of their decisions and to provide appropriate legal remedies to applicants. A 2012 proposal to shorten the time limits to 60/120 days has not yet been adopted, but would still allow twice the time currently allowed for the Pricing Council's decision-making.

23 See http://www.ncpr.bg/images/News/Tariff%20on%20the%20fees_exerpt_GS.pdf

24 Center for Corruption and Organised Crime Prevention, Bulgarian Council of Ministers, 2014. *Analysis of drug policy in the Republic of Bulgaria in order to prepare proposals against corruption practices.* At: http://borkor.government.bg/bg/page/462

algorithms; the number of patients with the condition; expenditure in the preceding year; and budgetary capacity. For some reimbursed products NHIF pays as little as 10% of the benchmark price.

43. As described above, for multi-source products containing the same INN in the same pharmaceutical form, the benchmark price is set with reference to the cheapest version of the product as determined by cost per DDD, and this is then pro-rated across all pack sizes. Benchmarking is also applied across different molecules within the same ATC subgroup where the products have been shown to be of similar efficacy and safety for treatment of a particular indication, in which case the benchmark or reference price is calculated according to the lowest cost/DDD within the cluster.[25]

44. Importantly, whether it is for multi-source products (i.e. containing the same INN in the same pharmaceutical form) or for a therapeutic class medicines grouped in a cluster, the level of NHIF reimbursement is then set as a proportion of the benchmark price, not the actual price. As a result, the OOP payment for a drug subject to, for example, 75% reimbursement may be considerably higher than 25% of the actual product's cost, if that product is not a benchmark-priced product. The patient's OOP costs consist of the reference price minus the NHIF contribution, plus any difference between the reference price and the retail price of the product. In many cases the actual price can be many times the benchmark price, and the NHIF contribution only a small fraction of the cost. This is said to be a key driver of patients seeking medicines without prescription, as the levels of reimbursement are often so low that it is cheaper to pay for the entire product OOP than to add the co-payment to the cost of seeing a doctor to obtain one.

45. There are also no co-payment exemptions for drugs. Such high private OOP expenditures suggest a mismatch between policy objectives for the NHIF – namely, limiting the funds' financial exposure – and that of providing financial protection and access to essential medicines.

46. **Table 4** illustrates the implications of this reimbursement method for ranitidine, a drug used in the treatment of oesophageal reflux and peptic ulcer disease, for which the level of reimbursement by the NHIF is 25%. The drug is available in 3 different forms on the market. For a treatment course corresponding to 30 days of 300mg/day (30 defined daily doses or DDDs), the patient will pay either BGN 5.96, 15.17 or 13.61 out of pocket, and the NHIF contribution will be only BGN 1.99 across all the products.

Table 4: Example of reimbursement for ranitidine (Annex 1 as of 12/12/2014)

	Ranitidin Tchaikapharma	Ranitidin Accord	Ranitidin Accord
Unit dose	**150mg tab**	**150mg tab**	**300mg tab**
Quantity in pack	20	30	30
Number of DDDs in the package	10	15	30
Retail price for package (BGN)	2.65	8.58	15.60
Reference price adjusted for amount of active ingredient	2.65	3.98	7.95
Amount paid by NHIF for package	**0.66**	**0.99**	**1.99**
Amount paid by NHIF for 30 DDD	**1.99**	**1.99**	**1.99**
Amount paid by patient for the package	**1.99**	**7.59**	**13.61**
Amount paid by patient for 30 DDD	**5.97**	**15.17**	**13.61**

2.5 Procurement and payment

47. For medicines used in in-patient facilities (Annex II) procurement procedures fall within the scope of the Public Procurement Act. Each public hospital undertakes the procurement annually. Prices cannot exceed those established by the Pricing Council. The costs of medicines used in hospitals are included in the estimations of the costs of the

25 Therapeutic reference pricing is not applied to medicines considered to have narrow therapeutic indices (eg anti-convulsants, immunosuppressants).

Clinical Care Pathways (CCPs), thus theoretically medicines for use in in-patients should be fully covered by hospital budgets. However patients with chronic diseases who receive medicines subsidized by NHIF in outpatient settings are expected to bring their medicines with them when hospitalized.

48. For outpatient medicines the NHIF is responsible for payment in accordance with the decisions of the Pricing Council and the specified levels of subsidy. It has no role in the disposition of the PDL, though representatives of NHIF attend meetings of the Pricing Council and may make representations to it.

49. In 2012, the MOH transferred responsibility for payment for a list of specialty medicines from it to the NHIF. These are 100% reimbursed and include certain oncology drugs funded outside the CCPs, as well as drugs for post-transplant immunosuppression, and various orphan diseases. Although additional funds were allocated to the NHIF for this purpose, increasingly they are insufficient to meet demand, and NHIF has only limited capacity to moderate prescribing. Expenditure on oncology medicines is one of the fastest growing areas of expenditure (56% growth rate over 2011-2013), and demand routinely outstrips the amounts budgeted. **Table 5** shows the magnitude and growth in NHIF medicines reimbursement over 2011-2013.

Table 5: Magnitude and growth in NHIF medicines reimbursement over 2011-2013

Group	Reimbursement value 2011 (000s, BGN)	Reimbursement value 2012 (000s, BGN)	Reimbursement value 2013 (000s, BGN)	Growth 2011-2013
Digestion and metabolism	92,808	104,748	117,120	26%
Blood & blood forming organs	32,825	31,318	43,739	33%
Cardiovascular	85,978	92,560	85,447	-1%
Genitourinary system	7,365	9,542	9,439	28%
Hormonal drugs for systemic use	4,275	6,078	6,803	59%
Anti-infectives for systemic use	9,586	13,760	14,695	53%
Antineoplastic & immunomodulatory drugs	57,207	72,331	88,998	56%
Musculoskeletal system	1,484	1,582	1,647	11%
Nervous system	76,840	70,245	61,120	-20%
Anti-parasitics	143	164	157	10%
Respiratory system	70,172	79,307	82,691	18%
Sensory organs	9,159	9,434	7,797	-15%
Various	5,237	7,740	8,484	62%
Monitors and test- strips	8,758	8,814	9,094	4%
Dietary foods	1,142	1,336	1,521	33%
Medical devices	10,184	10,652	11,253	10%
Total	**473,163**	**519,612**	**550,005**	**16%**

2.6 Distribution and supply chain

50. The Bulgarian pharmaceutical industry consists of around 30 domestic companies, and a number of international companies with local manufacturing/packaging, the largest of which is Actavis. All levels of distribution chain for medicines are highly regulated. Vertical integration (manufacturer - wholesaler - retailer) is theoretically prohibited.

51. The *Association of Research-based Pharmaceutical Manufacturers* in Bulgaria (ARPharM), established in 1996 represents the interests of 26 pharmaceutical manufacturers from Europe, US and Japan. \

52. The largest local producer is Sopharma, a founding member of the *Association of Bulgarian Pharmaceutical Manufacturers* (ABPhM), with both originator and generic products, and the only local manufacturer of sterile injectables in the country. Sopharma is in fact one of several entities reported to be heavily vertically integrated with a wholesaling operation as well as ownership of a large number of pharmacies.

53. There is also substantial horizontal integration. While one individual may only own a maximum of four pharmacies, the same individual may own multiple entities each of which may, in turn, also own up to four pharmacies, thereby facilitating control of a large network and creating scope for anti- competitive behaviour. One network of around 300 pharmacies is owned by a single entity, which also owns a wholesaler.

54. As of December 2014 there were 273 registered wholesalers in Bulgaria, with more than 320 warehouses. Although five wholesalers supply more than 80% of the market, this very large number is likely to be contributing to inefficiencies in the distribution chain.

55. Prescription medicines may only be dispensed and sold in pharmacies, whereas over-the-counter (OTC) medicines may be sold in both pharmacies and 'drug stores' (numbering 965 in 2010). As at January 2015 there were 4,217 registered pharmacies in Bulgaria, of which approximately half were authorized to dispense NHIF-subsidized prescriptions. However, only about half of these have contracts with NHIF permitting them to dispense fully reimbursed medicines (roughly one quarter of all registered pharmacies). Retail trade in reimbursable drugs is perceived as unattractive for a significant number of pharmacies, and in around 15% of Bulgarian municipalities there are no pharmacies dispensing NHIF-subsidized drugs at all.[21]

56. Because pharmacies do not receive dispensing fees for their professional services, they are heavily reliant on these retail margins, together with income from OOP prescription costs, and retail sales of OTCs and non-medical consumer goods. As noted previously, wholesale and retail mark-ups are set by the Ministry of Health, and are proportional to drug prices, which creates incentives to supply and/or dispense more expensive products. However, for drugs fully reimbursed by the NHIF[26], the retail markup is not applied, and pharmacies receive only a fee of 2 BGN per prescription (not per item) payable by the NHIF.

57. Consideration should be given to reducing the reliance of pharmacies on retail margins and eliminating disincentives for dispensing reimbursed products, by introducing a flat dispensing and/or professional service fee applicable to all NHIF subsidized prescriptions. This would also reinforce the role of pharmacists as highly trained health care professionals contributing to the safe and appropriate/rational use of medicines. Wholesale and retail margins should also be restructured so that they are at least partly unbundled from the prices of the medicines and replaced with fixed amounts, albeit with possible variations for products requiring special handling (for example, narcotics, cold chain, cytotoxics).

58. In addition, discounting at both the wholesale and retail level can skew the availability of particular products and create additional profits, because reimbursement is determined by list prices, not transaction costs. Consideration could be given to the introduction of a "clawback" policy based on mandatory disclosure of actual transaction prices, capturing cash and in-kind discounts. Both the UK and the Netherlands have instituted clawback arrangements where discounting in the supply chain and full price reimbursement create windfall profits.[27] Australia has also implemented a system of price adjustments for off-patent medicines based on mandatory disclosure of actual transaction prices (including cash and non-cash discounts), and this has led to very substantial price reductions in the off-patent market.[28]

2.7 Prescribing and dispensing

59. While drug prices are clearly an important determinant of overall expenditure, the other key components are prescribing practices and other influences on utilization. Industry promotion, formulary selection and design, clinical

26 All medicines in Annex II and III are fully reimbursed and selected medicines in Annex 1

27 In the UK and the Netherlands, policies allow the sharing of discounts between distributors and payers.

28 See http://www.pbs.gov.au/info/industry/pricing/eapd/price-disclosure-faq. Under this mechanism actual transaction costs – including cash and the value of discounts in kind - are required to be reported to Government for each product. At regular intervals the weighted average transaction prices are calculated, and the reimbursement prices adjusted downward to reflect these. In this way discounts that would otherwise be retained by pharmacies – by receiving discounted products but being reimbursed at the full rate – are captured by the Government.

guidelines, utilization management tools,[29] prescribing rules,[30] and co-payment policies are among important factors that influence demand. Promotion of new and more expensive medicines, prescriber detailing, and inducements to prescribers and pharmacists can contribute significantly to the rapid growth in the use of new and expensive therapies. Failure to promote the acceptance and use of generic medicines also increases expenditure.

60. Direct to consumer advertising of prescription medicines is not permitted, but pharmaceutical industry promotion to prescribers is thought to be influential in driving prescribing in favour of more expensive products. Anecdotally, there is strong and widespread criticism concerning the capacity of the BDA to adequately regulate pharmaceutical industry promotional activities.

61. Prescribing by INN is not encouraged in Bulgaria and for NHIF subsidized prescriptions, pharmacies must, at least in theory, dispense the brand specified by the prescriber. In practice however there is anecdotal evidence that because of the proportional nature of retail margins substitution does occur in favour of higher-priced products, and these are also favored where dispensing occurs without a prescription. The dispensing of prescription-only medicines to patients without prescriptions is driven in part by low and unpredictable rates of NHIF reimbursement and therefore of unpredictable OOP costs, but also because patients can avoid the cost and time of consulting a physician. While this presumably reduces costs to NHIF (while increasing out of pocket costs to patients) it could well be adding to the burden of medication-related adverse events and their associated costs, as well as to patterns of anti-microbial resistance.

62. Despite near universal prescribing by brand, and the prohibition on substitution at pharmacy for reimbursable drugs, generic utilization is substantial, though has been declining in recent years. Estimated at ~99% in 1989, the generic market share (by volume) decreased from ~99% in 1989 to ~76% in 2010, and in 2011 was at 75% by volume and 44% by value.[21] This may reflect the effect of originator industry promotional activities, but anecdotally is attributed, at least in part, to concerns about the quality of generic products. By specifying the originator brand in a prescription (without permitting substitution), prescribers believe their patients can avoid 'inferior' generic products. However, when a physician prescribes a medicine with a price higher than the reference or benchmark price, the patient must pay the difference out of pocket.

63. Although multisource drugs, irrespective of brand, are reimbursed to the same degree by NHIF, prescribing by brand is not necessarily cost neutral to NHIF, since brand preferences can lead to reduced competition, and incentives used to encourage brand preferences are reflected in higher prices for those drugs. These incentives – discounts and rebates – can generate substantials for pharmacies, and the benefits of competition are profits retained in the supply chain rather than lowering prices for patients and payers.

64. There are a number of ways to influence prescribing practices and promote the rational use of medicines. These include promoting or even mandating prescribing by INN and permitting substitution at pharmacy. Allowing substitution at pharmacy is an essential element in rational generic drug policy. Other mechanisms include applying constraints on prescribing—limiting the range or quantity of drugs or the circumstances in which they may be prescribed and/or reimbursed; requiring prescribers to adhere to predefined consensus / national clinical treatment guidelines[31] or specific treatment protocols or algorithms; imposing prescribing budgets that encourage or require prescribers to take cost and cost-effectiveness into consideration in making treatment decisions; introducing monitoring and feedback on individual prescribing patterns, with or without financial incentives or penalties; and academic detailing of physicians in clinical practice.[32] While academic detailing is an effective method of educating prescribers, it is highly resource intensive and

29 Examples include setting maximum quantities, imposing treatment algorithms, and requiring physicians to seek prior authorization to prescribe.

30 For example, mandating prescribing by INN.

31 To be effective in promoting efficient and rational care, clinical guidelines should take into account not just the comparative efficacy and safety of different therapies but also their cost effectiveness.

32 Academic detailing is form of face-to-face education for prescribers by trained health care professionals, typically pharmacists, physicians, or nurses. The goal of academic detailing is to change prescribing of targeted drugs to be consistent with available evidence, support patient safety, and to be cost-effective medication choices and overall, to improve patient care.

requires a substantial commitment to implement effectively. In addition, principles of rational prescribing could be introduced into undergraduate and postgraduate medical curricula. WHO has a number of well-tested materials on which such programs could be based.[33] Promoting rational prescribing should also be supported by the establishment of a source of independent drug information.

65. A requirement for INN-based prescribing should be accompanied with a communications strategy to promote patient and prescriber confidence in the quality of generics, together with labelling and packaging standards to minimize patient confusion when brand switching occurs. This should be coupled with the dissemination of information about the availability of least costly alternatives at pharmacies.

66. A framework should be established in which pharmacies are a) permitted to substitute (unless expressly ruled out on clinical grounds), b) both encouraged to offer and supply a benchmark-priced product, and c) penalized if they fail to do so when one is requested. One option would be for the NHIF to pay a small fee to the pharmacy when a benchmark-priced brand is supplied. [34]

67. Another option would be to require pharmacies to absorb any difference in cost if a patient requests a benchmark-priced product and one is not supplied. The difficulty with the latter is that where the drug is subject to co-insurance amount (as distinct from a flat co-payment) it can be difficult for the patient to know how much they should be paying. Pharmacies could, however, be required to display a list of benchmark prices for medicines in high-volume clusters, as a guide for patients.[35]

68. Where a benchmark-priced product is the one dispensed, no (or only minimal) co-payment should be required.[36] However, *if the patient chooses* an alternative brand, they should continue to bear the cost of any difference in price between the benchmark product and the one dispensed.

69. A policy framework requiring pharmacies to dispense benchmark-priced products on request must also ensure that such products are readily available to them. Matching incentives and penalties for wholesalers and distributors should also be considered.

2.8 Prices, utilization, expenditure

70. This section presents an analysis of prices, utilization and expenditure trends for selected drugs in Annexes I, II and III. In **Table 6** and **Table 8** Bulgarian prices are compared with prices in the UK and New Zealand for selected Annex I medicines, and for the Top 25 (by value) in Annex II (mainly high cost, patented oncology medicines) with prices in the UK alone. Where multiple prices are listed in the Annex for a given presentation the lowest price has been used for the comparison. It is important to note however that for some drugs the unit prices listed vary by more than a factor of 10 between different brands of the same presentation.

While for off-patent medicines better prices may be expected in the much larger and more competitive UK market, the same cannot be said for New Zealand, with a population of only 4.4 million.[37] For Annex II, UK prices were selected for the analysis because in the UK medicines are subject to an assessment of value for money by the National Institute for Health and Care Excellence (NICE).

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33 See for example http://apps.who.int/medicinedocs/en/d/Jwhozip23e/

34 This is a policy used effectively in Australia to encourage pharmacies to stock and dispense benchmark-priced products.

35 This would not be necessary with a system of flat co-payments (that is co-payments that do not vary with the cost of the drug, though they may vary with the patient's capacity to pay).

36 In some countries, co-payments are only required if a brand other than the lowest priced is selected. For example, in Germany, patients pay €5 out-of-pocket for a prescription, but if they accept a generic priced significantly below the market average under a contractual agreement between their insurance fund and the manufacturer, the co-payment may be waived.

37 The New Zealand Pharmaceutical Management Agency PHARMAC makes extensive use of sole supplier tendering for off patent products and the New Zealand market is highly competitive. The successful tenderer gets sole subsidized supply of the medicine for a fixed term thus creating maximum incentive to offer the best price

Table 6: Price Comparisons for Selected Medicines in Annex I

INN	Indication	Dose	Pack size	Level of NHIF Reimbursement	Bulgarian reference price (€)	NZ Price (€)	UK Price (€)	2013 NHIF Expenditure (€, 000s)
adalimumab	rheumatoid arthritis	40mg	2	75%	1047	1141	889	7,705.0
amlodipine	hypertension	10mg	30	50%	1.65	0.79	1.30	807.7
clopidogrel	anticoagulant	75mg	30	75%	3.28	1.24	16.38	2,113.0
enalapril	hypertension, heart failure	10mg	30	25%	1.23	0.28	1.31	755.0
etanercept	rheumatoid arthritis	25mg	4	75%	508	602	451	8,657.7
imiglucerase	Gaucher's disease	400U	1	100%	1,579	1,360	1,352	2,699.0
insulin glargine	diabetes	300IU	5	100%	53.26	59.92	52.36	3,939.0
insulin lispro	diabetes	300iU	10	100%	112	75.48	74.34	4,237.7
i**vabradine**	angina, heart failure	7.5mg	56	50%	57.95	N/A	50.68	2,765.7
latanoprost	glaucoma	125mcg	1	50%	3.92	1.26	2.25	1,684.1
lisinopril	hypertension	10mg	30	25%	2.57	0.86	1.31	926.5
metformin	diabetes	500mg	30	100%	0.47	0.23	3.60	3,192.3
metoprolol	hypertension	100mg	30	50%	2.29	1.53	1.43	1,073.5
olanzapine	antipsychotic	10mg	28	100%	2.56	1.62	1.83	3,214.0
salmeterol/ fluticasone	asthma	50/250mcg	60	100%	32.35	31.51	44.16	11,632.7
valsartan/ hctz	hypertension	160/12.5mg	28	50%	4.12	N/A	3.61	4,590.6
vildagliptin/ metformin	diabetes	50/1000mg	60	50%	47.38	N/A	42.87	3,248.4

NOTES: Text in bold denotes medicines in NHIF 'Top 25' by reimbursement value in 2014. Total expenditure is for all presentations and dosage forms of the INN. Data show NHIF expenditure, not total costs. Bulgarian prices shown as at 2 August 2014. Where multiple presentations listed, Bulgarian price shown is for product with lowest unit cost. All prices over 100 Euros are rounded. UK prices from http://www.ppa.org.uk/edt/September_2014/mindex.htm. NZ prices from http://www.pharmac.health.nz/tools-resources/ pharmaceutical-schedule. Some NZ and UK prices have been prorated to accommodate different pack sizes. Exchange rates as of 2 August 2014 from www.oanda.com

71. **Table 6** shows that there are a number of high unit cost, single source medicines for which Bulgarian prices may not reflect reasonable value for money. The prices of *adalimumab* and *etanercept*, for example, are 18% and 13% higher respectively, than in the UK. Further, in the UK their assessment by the National Institute for Health and Care Excellence (NICE) has resulted in use within the National Health Service being limited to the circumstances in which the drugs are considered cost effective. Bulgaria not only appears to be paying higher prices for these drugs (though this may in part be an artifact of the 20% VAT applied in Bulgaria) they are among those showing most rapid growth in expenditure (see **Table 7**) and the extent of any restrictions on usage is unclear.

Table 7: Top 25 Medicines in Annex I, by Value of NHIF Reimbursement in 2014

INN	Indication	2012 NHIF Expenditure (BGN)	2013 NHIF Expenditure (BGN))	2014 NHIF Expenditure (BGN)	Change Y-O-Y 2012-13	Change Y-O-Y 2013-14	Change 2012-14
adalimumab	rheumatoid arthritis	9,465,942	15,073,256	24,826,465	59%	65%	162%
salmeterol/fluticasone	asthma/COPD	22,831,674	22,757,030	23,364,372	0%	3%	2%
insulin aspart	diabetes	10,728,807	11,323,993	18,305,460	6%	62%	71%

insulin human	diabetes	18,249,329	16,651,920	17,944,348	-9%	8%	-2%
etanercept	rheumatoid arthritis	8,613,710	13,903,970	16,837,731	61%	21%	95%
budesonide/formoterol	asthma/COPD	24,263,812	25,144,791	15,780,278	4%	-37%	-35%
coagulation factor VIII	hemophilia	9,479,592	12,740,752	13,231,603	34%	4%	40%
tiotropium	COPD	14,858,952	15,411,605	12,366,567	4%	-20%	-17%
insulin lispro	diabetes	5,833,106	8,290,191	11,911,051	42%	44%	104%
interferon beta 1a	multiple sclerosis	9,111,680	9,965,819	10,037,138	9%	1%	10%
paliperidone	antipsychotic	4,333,022	7,706,792	9,454,521	78%	23%	118%
interferon beta 1b	multiple sclerosis	10,195,459	9,990,980	8,904,487	-2%	-11%	-13%
insulin glargine	diabetes	6,447,253	7,705,843	8,598,188	20%	12%	33%
beclomethasone/formoterol	asthma/COPD	-	-	8,543,773	-	-	-
deferasirox	thalassemia	6,897,317	7,507,064	7,597,220	9%	1%	10%
valsartan/HCTZ	hypertertension	6,878,636	8,980,669	7,513,336	31%	-16%	9%
vildagliptin/metformin	diabetes	5,645,987	6,354,738	7,496,976	13%	18%	33%
ticagrelor	acute coronary syndromes	597,799	4,194,705	6,692,876	602%	60%	1020%
insulin detemir	diabetes	4,919,898	5,449,875	6,432,483	11%	18%	31%
aripiprazole	antipsychotic	7,065,294	6,479,568	6,319,023	-8%	-2%	-11%
tafamadis	hereditary amyloidosis	N/A	1,625,885	6,233,366	-	283%	-
glatiramer	multiple sclerosis	4,503,186	4,712,093	6,085,895	5%	29%	35%
gliclazide	diabetes	5,783,239	5,873,388	5,976,307	2%	2%	3%
ivabradine	heart failure	4,516,473	5,410,449	5,878,187	20%	9%	30%
golimumab	rheumatoid arthritis	1,775,888	4,807,398	5,719,064	171%	19%	222%

Data supplied by NHIF. Note that figures shown are for NHIF reimbursement, not total cost

72. Similarly, while the prices of long-acting insulin analogs such as *insulin glargine* are comparable with those in the UK (notwithstanding the very substantial difference in per capita GDP and therefore capacity to pay), use of these products in the UK is largely limited to patients with Type I diabetes, as they are not considered cost effective in most patients with Type II diabetes. Others such as the TNFα inhibitors (eg *adalimumab, etanercept, infliximab*) are limited to third line therapy[38] and fourth line in Australia. [39]

73. Within Annex II there are also a number of drugs for which prices are similar to, and in some cases even higher than in the UK (**Table 8**). Currently drugs listed in Annex II carry no specifications as to the conditions for which they may be prescribed, though the addition of ICD codes reflecting the approved indications for marketing are planned.[40] Given that the UK has a PPP-adjusted per capita GDP more than twice that of Bulgaria, many of these drugs are clearly unlikely to be cost effective in Bulgaria. Many of these are also among those contributing most significantly to rapid expenditure growth. If the prices of just the four highlighted drugs – *nilotinib, rituximab*, *pazopanib* and *pemetrexed* – could be reduced to those in the UK, based on 2014 NHIF expenditure this alone would generate savings of BGN 10.8 milllion.

38 See https://www.nice.org.uk/guidance/ta130

39 See www.pbs.gov.au

40 However, these will reflect the scope of marketing approval, which for many drugs will be much broader than the conditions in which use of the drug is cost effective.

Table 8: Price comparisons for Top 20 medicines by value in Annex II*

INN	Brand	Dose	Pack size	Bulgarian wholesale price (€)	UK retail price (€)
bevacizumab	Avastin	400mg	1	1,185	1,274
trastuzumab	Herceptin	150mg	1	587	561
nilotinib	**Tasigna**	**200mg**	**28**	1,076	**838**
imatinib	Glivec	100mg	120	486	2,530
rituximab	**Mabthera**	**500mg**	**1**	1,453	**1,203**
pazopanib	**Votrient**	**N/A**	**N/A**	3,101	**772**
sunitinib	Sutent	25mg	30	2,488	2,317
bortezomib	Velcade	3.5mg	1	1,068	1,050
erlotinib	Tarceva	150mg	30	2,063	2,248
pemetrexed	**Alimta**	**500mg**	**1**	1,215	**1,102**
cetuximab	Erbitux	5mg/ml, 20ml	1	211	245
sorafenib	Nexavar	200mg	112	3,600	4,106
abiraterone	Zytiga	250mg	120	3,687	4,037
panitumumab	Vectibix	100mg	1	427	523
pegfilgrastim	Neulasta	6mg	1	877	946
everolimus	Afinitor	10mg	30	3,601	4,092
denosumab	Xgeva	120 mg/1.7ml	1	358	427
romiplostim	Nplate	250mcg	1	626	664
vemurafenib	Zelboraf	240mg	56	2,439	2,411
cabazitaxel	Jevtana	60mg	1	4,606	5,092

NOTES: Bulgarian prices as at 15 March 2015. Where multiple presentations are listed, the Bulgarian price shown is for the product with the lowest cost/DDD. All prices over 100 Euros are rounded. UK prices from British National Formulary, March 2015. Exchange rates as of 1 March 2015 from www.oanda.com. Some UK prices have been pro-rated to accommodate different pack sizes.

74. Moreover many of the medicines list in **Table 8** and **Table 9** are subject to very significant constraints in use in the UK, or not approved for use on the NHS. For example, NICE does not recommend *bevacizumab* for use in any solid tumours; *sunitinib* is only recommended for first line and *sorafenib* is not recommended for either first or second line treatment in renal cell carcinoma. Many of the other drugs listed here are very significantly restricted in the UK to ensure cost effective use. There is no evidence that such restrictions are applied in Bulgaria (in the absence of official guidelines).

75. A more extensive review of the existing PDL is likely to reveal further examples of drugs unlikely to be cost effective at current Bulgarian prices, especially where existing clinical treatment algorithms do not take into account the cost effectiveness of different therapies. Absent very significant reductions in price, several drugs are likely to require very tight restrictions in order to approach cost effectiveness, or otherwise be considered as candidates for disinvestment (delisting).

Table 9: Top 25 Annex II medicines by value of NHIF expenditure, and growth in outlays over 2012-2014

INN	Indication	2012 NHIF Expenditure (BGN)	2013 NHIF Expenditure (BGN)	2014 NHIF Expenditure (BGN)	Change Y-O-Y 2012-13	Change Y-O-Y 2013-14	Change 2012-2014
bevacizumab	multiple cancers	10,542,387	22,655,540	32,364,113	115%	43%	207%
trastuzumab	HER2+ breast cancer	19,213,305	25,737,247	28,066,820	34%	9%	46%
nilotinib	chronic myeloid leukemia	7,365,426	11,001,962	13,237,985	49%	20%	80%
imatinib	chronic myeloid leukemia, GI stromal tumor	12,522,185	12,713,847	9,963,545	2%	-22%	-20%
rituximab	non-Hodgkins lymphoma	6,573,673	8,902,784	9,564,990	35%	7%	46%
pazopanib	renal cell carcinoma, soft tissue sarcoma	2,234,502	5,636,499	7,478,311	152%	33%	235%
sunitinib	renal cell carcinoma, GI stromal tumor	4,451,781	6,158,572	7,302,621	38%	19%	64%
bortezomib	multiple myeloma	3,363,275	6,155,061	7,077,786	83%	15%	110%
erlotinib	non small cell lung cancer	2,622,949	5,114,310	6,959,394	95%	36%	165%
pemetrexed	non small cell lung cancer	3,752,392	4,997,414	6,128,684	33%	23%	63%
cetuximab	colorectal cancer	1,869,311	2,878,789	5,850,361	54%	103%	213%
sorafenib	renal cell carcinoma, liver cancer	2,997,950	4,679,733	5,547,446	56%	19%	85%
abiraterone	hormone refractory prostate cancer	-	-	6,421,158	-	-	-
panitumumab	colorectal cancer	2,347,526	3,834,203	5,565,627	63%	45%	137%
pegfilgrastim	granulocyte colony stimulating factor	2,121,336	3,639,723	5,220,313	72%	43%	146%
everolimus	immunosuppression post organ transplant	1,728,260	2,011,974	5,101,729	16%	154%	195%
denosumab	osteoporosis, bone metastases	-	723,940	4,727,351	-	540%	-
romiplostim	thrombocytopenia	1,394,614	2,204,425	3,613,386	58%	64%	159%
vemurafenib	melanoma	-	-	3,194,221	-	-	-
cabazitaxel	hormone refractory prostate cancer	-	-	3,180,139	-	-	-
lapatinib	breast cancer	1,442,569	2,323,999	3,085,399	61%	33%	114%
zoledronic acid	osteoporosis, bone metastases	9,575,436	9,025,084	2,171,856	-6%	-76%	-77%
dasatinib	chronic myeloid leukemia	2,409,378	2,581,825	2,829,186	7%	10%	17%
gefitinib	non small cell lung cancer	654,512	2,069,502	2,290,891	216%	11%	250%
octreotide	growth hormone producing tumors	1,184,774	1,817,878	2,326,564	53%	28%	96%

Table 10: Price comparisons for Annex III

INN	Brand	Dose	2013-14 price in Bulgaria (€)	Current price in UK (€)
lopinavir/ritonavir	Kaletra	200mg/50mg x 120	403.68	358.39
abacavir/lamivudine	Kivexa	600mg/300mg x 30	330.68	375.97
tenofovir disoproxil	Viread	245mg x 30	342.23	256.65
methadone	Metadon	10mg/ml x 100ml	4.98	17.45
darunavir	Prezista	600mg x 60	668.95	560.93
emtricitabine	Emtriva	200mg x 30	164.82	174.52
atazanavir	Reyataz	150mg x 60	404.86	380.96
lamivudine/zidovudine	Combivir	150/300mg x 60	248.21	320.33
raltegravir	Isentress	400mg x 60	711.53	591.95
saquinavir	Invirase	500mg x 120	277.61	315.51
rifampicin	Tubocin	300mg x 100	15.53	59.27
ritonavir	Norvir	100mg x 30	24.32	24.41
etravirine	Intelence	100mg x 120	428.52	378.31
efavirenz	Stocrin	200mg x 90	67.39	251.48
fosamprenavir	Telzir	700mg x 60	302.44	276.42
pyrazinamide	Pyrazinamide Krka	500mg x 100	10.07	131.22
ethambutol	Ethambutol-Milve	250mg x 50	2.15	32.29
maraviroc	Celsentri	300mg x 60	763.95	554.11
nevirapine	Nevirapine Teva	200mg x 60	86.77	153.20
lamivudine	Epivir	150mg x 60	77.79	152.97
zidovudine	Retrovir	100mg x 100	94.46	111.58
didanosine	Videx	400mg x 30	147.19	193.62
isoniazid	Isonid	100mg x 100	1.22	64.58
lopinavir/ritonavir	Kaletra	100mg/25mg x 60	100.92	96.50
lopinavir/ritonavir	Kaletra	(80 mg/20 mg)/ml - 60 ml x 5	74.22	385.99
enfuvirtide	Fuzeon	108mg x 60	1214.74	1358.43

NOTES: Bulgarian prices from 2013/14 contracts. UK prices from British National Formulary, March 2015.
Exchange rates as of 1 December 2014 from www.oanda.com. Some UK prices have been pro-rated to accommodate different pack sizes.

Table 11: Expenditure trends, Annex III, 2011/12 – 2013/14

INN	Brand	Dose/ Quantity	Price with VAT (BGN)	2011-12 Aggregate Value	2012-13 Aggregate Value	2013-14 Aggregate Value	Change Y-O-Y 2011/12-2012/13	Change Y-O-Y 2012/13-2013/14	Change 2011/12-2013/14
lopinavir/ritonavir	Kaletra	200/50mg x 120	793.81	1,268,032	1,201,603	2,032,159	-5%	69%	60%
abacavir/	Kivexa	600/300mg x 30	650.26	1,450,863	1,417,558	1,762,844	-2%	24%	22%
tenofovir	Viread	245mg x 30	587.76	577,410	1,043,780	1,572,875	81%	51%	172%
methadone	Metadon	10mg/ml,100ml	9.52	551,652	590,488	996,039	7%	69%	81%
darunavir	Prezista	600mg x 60	0.04	252,038	433,215	891,743	72%	106%	254%
emtricitabine	Emtriva	200mg x 30	324.11	241,388	469,289	717,597	94%	53%	197%
atazanavir	Reyataz	150mg x 60	796.12	495,995	543,764	714,912	10%	31%	44%
lamivudine/	Combivir	150/300mg x 60	488.09	740,737	738,196	679,418	0%	-8%	-8%
raltegravir	Isentress	400mg x 60	1399.16	17,517	122,554	453,328	600%	270%	2488%
saquinavir	Invirase	500mg x 120	545.90	423,419	364,784	443,820	-14%	22%	5%
rifampicin	Tubocin	300mg x 100	30.53	217,073	196,606	217,087	-9%	10%	0%
ritonavir	Norvir	100mg x 30	47.83	119,446	75,518	211,961	-37%	181%	77%
etravirine	Intelence	100mg x 120	842.64	23,594	45,840	171,899	94%	275%	629%
efavirenz	Stocrin	200mg x 90	132.52	113,490	147,686	157,562	30%	7%	39%
fosamprenavir	Telzir	700mg x 60	594.72	131,286	116,565	117,160	-11%	1%	-11%
pyrazinamide	Pyrazinamide Krka	500mg x 100	19.80	82,823	102,263	82,823	23%	-19%	0%
ethambutol	Ethambutol-Milve	250mg x 50	4.23	84,169	74,466	75,840	-12%	2%	-10%
maraviroc	Celsentri	300mg x 60	1502.24	5,723	7,565	66,098	32%	774%	1055%
nevirapin	Nevirapine Teva	200mg x 60	170.62	60,307	28,650	56,172	-52%	96%	-7%
lamivudine	Epivir	150mg x 60	152.96	103,759	83,205	49,713	-20%	-40%	-52%
zidovudine	Retrovir	100mg x 100	185.75	10,480	29,983	35,478	186%	18%	239%
didanosine	Videx	400mg x 30	0.02	101,457	71,719	30,644	-29%	-57%	-70%
isoniazid	Isonid	100mg x 100	2.40	27,041	27,072	27,137	0%	0%	0%
lopinavir/ritonavir	Kaletra	100/25mg x 60	198.45		6,853	10,207	-	49%	-
lopinavir/ritonavir	Kaletra	(80/20 mg)/ml,	145.94		2,184	22,725	-	941%	-
enfuvirtide	Fuzeon	108mg x 60	2388.68	75,188	5,494	4,777	-93%	-13%	-94%

In January 2015 thirteen new medicines were added to the PDL, with a total estimated expenditure of BGN 34.6 million in the first year. While some of these costs will be offset by reductions in the use of other medicines, this represents a substantial financial outlay for the NHIF. These are shown in Table 12.

Table 12: Prices and forecast expenditure for new drugs listed on the PDL on 1 January 2015

INN	Dose/Qty	BGN price (€)	UK Retail Price (€)	Forecast expenditure BGN (2015)
ruxolitinib	5mg x 56	2,158	2,155	11,428,200
pertuzumab	30 mg/mL 14ml	3,239	3,071	8,895,050
axitinib	5mg x 56	4,074	4,510	3,332,784
aflibercept	25mg/mL, 4mL	383	379	1,782,000
lixisenatide	10mcg x 14	41.99	34.72	1,765,536
afatinib	30mg x 28	2,159	2,595	1,276,122
vandetanib	300 mg x, 30	N/A	6,412	1,187,926
fluticasone/vilanterol	22mcg x 30	41.25	35.65	1,029,216
lipegfilgrastim	6mg/0,6ml x 1	875	N/A	1,026,732
brentuximab	50-mg vial =	3,730	3,206	903,000
crizotinib	250x 60	5,714	6,013	712,958
pasireotide	0.3mg x 60	3,305	3,591	670,000
apomorphine	10 mg/ml, 5ml	240	187	622,134
			Total	**34,631,658**

NOTES: Bulgarian prices from Annex II dated 16 March 2015. UK prices from British National Formulary, March 2015.
Exchange rates as of 1 January 2015 from www.oanda.com. Some UK prices have been pro-rated to accommodate different pack sizes.

76. Table 12 shows that the prices of these drugs in Bulgaria are comparable to those in the UK, yet several of them are either not considered cost effective there or are significantly restricted in their use on the NHS. Many of these new listings are therefore unlikely to be cost effective options for Bulgaria at this time.

- *ruxolitinib* is a selective inhibitor of the Janus-associated tyrosine kinases JAK1 and JAK2 and is licensed for the treatment of disease-related splenomegaly or symptoms in patients with primary myelofibrosis, post-polycythaemia vera myelofibrosis, or post-essential thrombocythaemia myelofibrosis. However ruxolitinib is *not recommended by NICE* for any of these conditions.[41]
- *pertuzumab* is used in combination with trastuzumab and docetaxel for the treatment of HER2 positive metastatic or locally recurrent unresectable breast cancer which has not been previously treated, or has relapsed after adjuvant therapy. NICE's appraisal committee *did not recommend* the technology because the incremental cost effectiveness ratio (ICER) was in excess of £125,000 per quality-adjusted life-year (QALY).[42]
- *axitinib* is recommended by NICE as an option for treating adults with advanced renal cell carcinoma after failure of treatment with a first-line tyrosine kinase inhibitor or a cytokine, *only if the company provides axitinib with the discount agreed in the patient access scheme.* In other words, the drug is only considered satisfactorily cost effective in the UK at a discount on the listed price.[43]

41 www.nice.org.uk/TA289

42 www.nice.org.uk/guidance/gid-tag322/documents/breast-cancer-her2-positive-metastatic-pertuzumab-with-trastuzumab-and-docetaxel-dsu-spec-assessing-technologies-that-are-not-cost-effective-at-a-zero-price2

43 www.nice.org.uk/guidance/ta333, www.nice.org.uk/guidance/ta333/documents/renal-cell-carcinoma-advanced-axitinib-final-appraisal-determination-document2

- *aflibercept* in combination with irinotecan and fluorouracil-based therapy is *not recommended by NICE* for the treatment of metastatic colorectal cancer that is resistant to or has progressed after an oxaliplatin-containing regimen.[44]
- *afatinib* is a protein kinase inhibitor licensed for the treatment of locally advanced or metastatic non-small cell lung cancer with activating epidermal growth factor receptor (EGFR) mutations, in patients who have not previously been treated with an EGFR tyrosine kinase inhibitor. Afatinib is recommended by NICE for treating locally advanced or metastatic non-small-cell lung cancer in adults:whose tumour tests positive for the epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation, who have not previously had an EGFR-TK inhibitor, *and if the manufacturer provides afatinib with the discount agreed in the patient access scheme.*[45]
- *brentuximab* is licensed for the treatment of relapsed or refractory CD-30 positive Hodgkin's disease following autologous stem cell transplant or following at least two prior therapies, when autologous stem cell transplant or multi-agent chemotherapy is not a treatment option. It is also licensed for relapsed or refractory systemic anaplastic large cell lymphoma. It has not yet been considered by NICE.[46]
- *lipefilgrastim* has not yet been considered by NICE, but the Scottish Medicines Consortium found it *non-inferior to pegfilgrastim* and accepted it for restricted use within NHS Scotland.[47]
- *lixisenatide* is used in people with type 2 diabetes who are receiving oral antidiabetic drugs or basal insulin. Efficacy is assessed by measuring levels of glycosylated haemoglobin (HbA1c), however non-inferiority to exenatide (already listed) has not been shown for this outcome and there are as yet no published data relating to clinical endpoints.

3. Analysis and Recommendations

77. Without an integrated national medicines policy, the Bulgarian pharmaceutical sector is characterized by various highly prescriptive and at times, arguably counterproductive policy levers. While the regulatory framework has been largely brought into line with current EU standards, existing mechanisms for listing, pricing and subsidizing medicines are not ensuring adequate value for money for the NHIF, and are contributing to inefficiencies in the public financing of the health sector. Current pharmaceutical policy settings appear focused on limiting NHIF outlays rather than rather than prioritizing access and affordability, and afford little financial protection to patients.

78. Processes for listing medicines on the Positive Drug List are insufficiently influenced by considerations of cost effectiveness and there are no explicit links between circumstances of listing and existing prescribing practices. Insufficient consideration of cost-effectiveness when listing and pricing medicines together with inadequate or ineffective restrictions on prescribing are resulting in rapid growth in public expenditure on some very high unit cost and potentially non cost-effective medicines. A significant portion of this rapidly growing expenditure is avoidable.

79. Current policy settings do not promote competition among off-patent medicines and many prices for both patented and off-patent medicines compare unfavorably with countries with far greater capacity to pay. Several high cost medicines contributing significantly to rapid expenditure growth are unlikely to be cost effective in Bulgaria and should be subject to price (re)negotiation, explicit restrictions on use, and in some cases, disinvestment (delisting).

80. Ideally, a key objective of any reforms should be to improve overall coverage of essential prescription medicines and reduce OOP costs for patients, taking into account the existing and evolving burden of disease in setting expenditure priorities. If Bulgaria were also able to encourage greater competition in the off-patent medicines market,

44 www.nice.org.uk/guidance/ta307/chapter/1-guidance

45 www.nice.org.uk/TA310

46 www.nice.org.uk/guidance/indevelopment/gid-tag467

47 www.scottishmedicines.org.uk/SMC_Advice/Advice/908_13_lipegfilgrastim_Lonquex/lipegfilgrastim_Lonquex

this, together with measures to address demand and promote rational prescribing and generic uptake, could significantly improve efficiency in current pharmaceutical expenditure.

81. More rational processes for drug evaluation are critical, as are procurement and pricing mechanisms that are more flexible and fit for purpose, and can effectively leverage the market power of the public sector by utilizing inclusion on the PDL as an effective barrier to market entry. These would include giving the Pricing Council the capacity to negotiate prices with pharmaceutical manufacturers and to introduce risk-sharing arrangements, bundling agreements and other approaches to pricing beyond the passive acceptance of prices reported in other countries.

3.1. Goal: Greater clarity in policy objectives

- *Prioritize the development of a comprehensive, integrated, national medicines policy*

82. The *Concept Note: Health 2020 Goals*[48] stresses the importance of increasing the efficiency of drug treatment, of building capacity for the evaluation of health technologies, of the role of clinical guidelines and treatment algorithms, and of prescribing and using medicines that are effective and cost-effective. It articulates the need for improvements in the mechanisms for pricing and reimbursement of medicinal products and medical products paid for with public resources.

83. While these are critical policy goals they do not capture all the elements necessary to articulate a comprehensive national medicines policy. Although there has been some considerable support for the development of an overarching policy, previous attempts to develop one have stalled.

84. It is recommended that the Bulgarian Government prioritize the development and promulgation of a comprehensive national medicines policy, with clear objectives and priorities addressing financing, equity of access, individual and collective affordability and financial protection, technical and allocative efficiency, and long term sustainability. All relevant stakeholders should be represented in its development through a consultative process, and should commit to supporting it once agreed.

3.2 Goal: More effective formulary decision making and pricing processes

Consider

- *revising the remit, structure, composition and operation of the National Pricing Council*
- *introducing (comparative) cost effectiveness as a mandatory criterion for inclusion of a drug in the PDL*
- *establishing a simplified HTA process until HTA resources and mechanisms can be established*
- *modifying use of external reference pricing pending implementation of full HTA*
- *introducing competitive tendering for off patent medicines, both for individual molecules and selected therapeutic classes; limiting the number of products and suppliers; and requiring supply guarantees*

Introduce mandatory Budget Impact Assessment for all new medicines with anticipated high cost or utilization

Review the current PDL and consider delisting or restricting products unlikely to be cost effective in Bulgaria; renegotiate prices where possible

Consider applying restrictions on listing, and developing risk sharing arrangements (RSAs) for high cost medicines

Progress development of evidence-based clinical treatment guidelines that take into account the cost effectiveness of therapies in Bulgaria.

48 At www.mh.government.bg/Articles.aspx?lang=bgBG&pageid=472&home=true&categoryid =7573

85. The operation of the Pricing Council should be revised as a matter of priority to a) modify its remit, b) provide it with needed expertise, c) clarify evaluation and decision criteria, d) improve the transparency and quality of decision-making, and (e) enable engagement with stakeholders.

86. The procedural and governance arrangements of the Pricing Council and reimbursement program should ensure that a recommendation for the addition of a medicine to the PDL cannot be made in the absence of an evidence-based evaluation of effectiveness and cost-effectiveness, budget impact assessment (BIA), and specific consideration of the necessary conditions for cost-effective prescribing. Medicines should only be added to the PDL if they can be shown to reflect reasonable value for money in the Bulgarian context. BIA should be undertaken using epidemiological estimates, taking into account current or anticipated prescribing patterns.

87. Detailed information about the considerations of the committee and the evidence that has informed its recommendations should be published and prescribers should encouraged to understand the relative merits and costs of medicines, particularly as detailing by pharmaceutical companies will tend to exaggerate benefits and downplay risks (including expenditure risks).

88. Core principles that should be codified in guidelines for the future operation of the Pricing Council should include

- *Independence* from government, MoH, NHIF, sectoral interest groups (including clinical and patient groups) and industry, by recognizing any conflict of interest in policies and processes for engaging with different stakeholders.
- *Transparency* in the way work is prioritized, the evidence synthesized and assessed, and the final decisions made; by publicizing all relevant analyses; and by minimizing the extent to which information is protected.
- *Scientific rigour*, by applying peer review and remaining methodologically current in the evaluation of evidence.
- *Value and affordability*, by ensuring that comparative cost effectiveness is an essential criterion for a positive listing decision.

89. Membership of the Pricing Council should include clinicians representing the key internal medicine specialties, one or more representatives of primary care, at least one health economist, and one or more consumer representatives. It could also include a pharmacist, and an epidemiologist/ biostatistician.

90. While the availability of legal expertise is essential to the Pricing Council's effective operation, it is not clear that legal practitioners are needed for formulary decision making *per se*, particularly where decisions rely on assessments of clinical and cost effectiveness rather than legal precepts. The Pricing Council need not undertake explicit evaluation of applications for listing of generic versions of already-listed medicines; these could be processed by Secretariat staff.

91. The time taken to review and consider applications for listing and pricing is well short of the maximum duration specified in the EU Transparency Directive and may not be sufficient to allow for rigorous assessment of an application dossier. The frequency of meetings of the Council would also need to be modified to reflect the changes in process. Consideration should be given to increasing Application fees to support an expansion of resources and to more closely reflect the effort required to manage the listing and pricing processes. Experience from other countries suggests that the PDL and price could be updated less frequently, for instance once or twice a year.

92. When medicines are listed on the PDL sponsors should be required to guarantee availability of sufficient product to supply a minimum percentage of the anticipated market at or below the price proposed, for at least 12 months. Under the current arrangements a product can be accepted for listing on the PDL and set the benchmark, and yet be largely unavailable, thus increasing patient OOP costs.

93. A key recommendation is the introduction of full health technology assessment (HTA) for medicines (and potentially for other health technologies) as a specific medium term objective (3-5 years). A key part of the establishment of the process will be the development of guidelines both for applications to the process and those involved in their evaluation. Guidelines for the submission of applications for consideration by the committee are currently being drafted;

these should set forth in some detail the nature, scope, presentation, rigour and transparency expected of the evidence of comparative clinical and cost effectiveness to be presented by the applicants. Above all, the establishment of cost effectiveness as a mandatory criterion for listing of a drug on the PDL must be prioritized.

94. Establishing an HTA framework will take time and resources but Bulgaria may be able to draw on the experience of other EU member states. Several smaller countries are well advanced in establishing HTA processes and entities, and there are potential opportunities for synergy and collaboration. A good example is the introduction of the Baltic pharmacoeconomic guidelines and combined evaluation processes.

95. In the interim an abbreviated HTA process could be introduced using a scoring mechanism that draws on the extent to which a medicine has been subject to HTA and the conditions under which it is reimbursed elsewhere in the EU. A simple scorecard similar to that previously proposed by *Seiter* (2007)[49] could be developed and use to support decisions on whether (and the extent to which) a product should be included in the PDL. The current regulations specify that a new medicine must be reimbursed in at least 5 other jurisdictions, but it need not have been subject to HTA.

96. In addition, until HTA can be put in place to directly or indirectly influence pricing, it is suggested that a modified external reference pricing paradigm be adopted. Under this paradigm, the price of a new medicine would be determined based on the price of that medicine in an EU country (Country A) where it has been reimbursed following rigorous HTA review, adjusted by factor equivalent to the ratio of Bulgarian GDP to Country A GDP (PPP adjusted). This adjusted price then forms the target price for negotiation with the drug's sponsor. Subsequent inclusion of the medicine on the Bulgarian PDL based on this adjusted external reference price should be limited to those indications and treatment settings for which it is reimbursed in Country A.

97. Undertaking an in-depth review of the current Annexes could free up some resources relatively quickly. All high unit cost and high volume products on the Reimbursement List would be reviewed to determine whether reimbursement should be restricted in terms of indications, patient populations, prior treatment modalities, treatment duration and/or maximum quantities, to support cost-effective use. Prior authorization should be required for all drugs for which diagnostic certainty or prior treatment failure is a prerequisite for cost-effective therapy. This could be expedited by mirroring any listing conditions applying in the country from which the price has been referenced and requiring the negotiation of RSAs for all products for which expenditure has exceeded a pre-determined threshold in the preceding financial year.

98. The use of BIAs should guide the introduction and use of financial Risk Sharing Arrangements (RSAs). Estimating the size of the population in whom the drug is likely to be cost effective can inform the terms and parameters of an RSA. Absolute expenditure caps (with rebates for use exceeding agreed estimates) could be considered in cases where anticipated utilization is difficult to estimate) or price-volume agreements (where unit prices are reduced beyond an agreed volume) where cost-effectiveness differs between sub-populations, and where use cannot easily be limited to cost-effective settings. RSAs can improve the accuracy of budget impact assessments and discourage inappropriate promotion both to prescribers and within the distribution chain. Uptake should be monitored with regular review of observed *vs* expected utilization.

99. It is recommended that in order to optimize pricing for high volume off-patent medicines, consideration be given to limiting reimbursement to one, or at most two or three brands of any molecule, selected on the basis of open tender. Successful tenderers should be required to demonstrate that they are able to supply a pre-specified proportion of the market as a minimum, and penalties should be established and enforced for failure to supply.

100. Limiting the number of suppliers of a given molecule will encourage competition in the market; the greater the proportion of the market guaranteed for a given supplier the steeper the price reductions likely to be achieved. If

[49] Seiter A. *A Practical Approach to Pharmaceutical Policy* [Internet]. The World Bank; 2010. Available from: http://elibrary.worldbank.org/doi/book/10.1596/978-0-8213-8386-5

necessary to retain low turnover products on the market, consideration could be given to exemptions from BDA fees (on a rebate basis) for low volume/ low value medicines, including orphan drugs.

101. For (high volume and high cost) classes within which there is a high degree of therapeutic interchangeability (eg proton pump inhibitors, ACE-inhibitors, angiotensin receptor blockers, statins, calcium channel blockers), consideration should be given to limiting subsidy to no more than two, or at most three molecules in each class, again on the basis of competitive tendering. Successful tenderers should again be required to provide supply guarantees, with penalties applying for supply failures. For some high unit cost drugs for example erythropoietins, sole supply arrangements could even be considered. This would create a strong incentive for competitive pricing. In a resource constrained environment choice might reasonably be considered a luxury; it is difficult to imagine why six erythropoiesis stimulating agents (ESAs) are needed.

3.3 Goal: improved access, equity, and affordability

Consider

- *replacing co-insurance with fixed, flat co-payments*
- *introducing a consumer awareness campaign to reinforce a) the safety and quality of generic medicines; b) the actual costs of medicines; and c) opportunities for consumers to save money at the pharmacy by choosing benchmark-priced products*
- *using savings on off patent medicines to increase levels of reimbursement in key therapeutic classes*

102. An active generics policy also requires undertaking awareness campaigns to encourage widespread acceptance for generic medicines among patients and prescribers. A program to promote the safety and quality of generic medicines, raise awareness of actual costs of medicines and opportunities to save money by choosing generic options at pharmacy should be developed. The actual price of a medicine could be added to the dispensing label. This encourages consumer awareness of the value of the subsidy provided.

103. Rationalization and simplification of patient co-payments through the introduction of a flat co-payment structure should be considered to improve both equity and individual affordability. Co-insurance is regressive and creates uncertainty for patients; uncertainty in cost has been shown to reduce treatment adherence. This need not involve increased expenditure; it should be possible to model a tiered co-payment system that is revenue neutral.

104. Further improvements in affordability could be achieved by educating prescribers in cost effective prescribing, ensuring the availability of benchmark priced products at pharmacy, and by raising awareness among consumers of the safety, quality and availability of generic medicines and the additional costs that may be avoided by choosing a benchmark-priced product.

3.4 Goal: Better management of utilization and promotion of rational use

- *Develop and mandate adherence to clinical guidelines based on evidence of effectiveness and cost effectiveness*
- *Consider introducing "good prescribing" education for prescribers, which should an understanding of the comparative effectiveness and cost effectiveness of treatments*
- *Consider introducing indicative individual prescribing budgets, with monitoring of prescribing behavior and feedback to prescribers*
- *Consider introducing an entity to provide independent drug information*

105. Evidence-based consensus guidelines are needed to guide rational pharmacotherapy nationally. Currently guidelines are being developed that are not informed by considerations of cost or cost effectiveness, and may lead to greater expenditure by encouraging uptake of new treatments. .

106. In addition to clinical guidelines, physicians need to be educated on the principles of rational prescribing. This education should be offered to medical students, recent graduates and as part of continuing professional education.

107. Consideration should be given to introducing indicative prescribing budgets in primary care, with accompanying mechanism to monitor prescribing and provide constructive feedback to prescribers.

108. Finally consideration could be given to the establishment of an entity involving academics and health professionals to provide a source of independent drug information. This could also undertake academic detailing and support training and curriculum development in rational prescribing.

3.5 Goal: Improved distribution chain

Consider

- *permitting substitution at pharmacy for NHIF-reimbursed medicines*
- *establishing incentives for pharmacies to dispense benchmark-priced generics and for wholesalers to supply them*
- *introducing fees for professional services eg dispensing*
- *introducing fixed, flat wholesale and retail margins*
- *introducing clawback arrangements to take advantage of discounting in the distribution chain*

109. As pharmacies do not receive dispensing fees or any other payments for professional services (apart from a 2BGN fee in lieu of a co-payment paid by the patient for a prescription containing up to three fully reimbursed items) pharmacies rely on income from dispensing without prescription, OOP prescription costs, dispensing higher priced products where possible, margins on retail sales of OTCs and non-medical consumer goods. In addition significant income is likely to accrue from discounting in the supply chain.

110. Reducing the dependence of pharmacies on income from retail margins, and giving financial recognition for professional services would lessen this reliance and reinforce the role of the pharmacist as a health care professional contributing to the safe and appropriate use of medicines. Pharmacists are highly trained professionals in Bulgaria, undertaking up to five years of tertiary study and this investment should be capitalized on.

111. A framework could be established in which pharmacies are both encouraged to offer and supply a benchmark-priced product and penalized if they fail to do so when one is requested. One option would be to introduce a small dispensing fee payable when a benchmark price brand is supplied. Another option would be to require the pharmacy to absorb any difference in cost if the patient requests a benchmark-priced product and one is not supplied. The difficulty with the latter is that with co-insurance rather than fixed co-payments it is difficult for a patient to know where the benchmark is. Pharmacies could however be required to display a list of benchmark prices for medicines in high volume clusters, as a guide for patients. A policy that requires pharmacies to dispense a benchmark product on request must also ensure that such products are available to them. Matching incentives and penalties for wholesaler and distributors would also need to be developed.

112. The current structure of the wholesale and retail margins creates incentives to supply and dispense more expensive drugs, and to reduce availability of cheaper ones. Wholesale and retail margins should be restructured so that they are unbundled from the prices of the medicines and replaced by fixed amounts, with variations for products requiring special handling (e.g., narcotics, cold chain, cytotoxics).

113. In addition significant discounting at both wholesale and retail level skews the availability of particular products and creates additional profits as prescriptions are reimbursed based on the list prices. Consideration could be given to the introduction of a clawback policy based on mandatory disclosure of actual transfer prices, taking into account cash and non-cash discounts.

3.6 Goal: A more sustainable system

Consider

- *reducing VAT to the concessional rate*
- *requiring supply guarantees to discourage parallel exports*
- *adjusting prices across the board if expenditure growth exceeds GDP growth*

114. As noted above VAT on medicines in Bulgaria is substantially higher than many other EU countries. Where patients face significant OOP costs, VAT on medicines differentially affects the poor and contributes to inequity. It is recommended that consideration be given to reducing the VAT rate to a level similar to other CEE countries.

115. Efforts to reduce prices carry the risk of encouraging parallel exports. Anecdotally, this is said to be a significant issue, but data were not available. Parallel exports are difficult to track, and a recent constitutional court decision nullified requirements approved by the Parliament in 2014 that introduced authorization by BDA of any planned export of medicines included in the PDL.[50] The key risk of parallel export is the potential for shortages of essential medicines. One option would be to require supply guarantees as a condition of inclusion on the PDL.

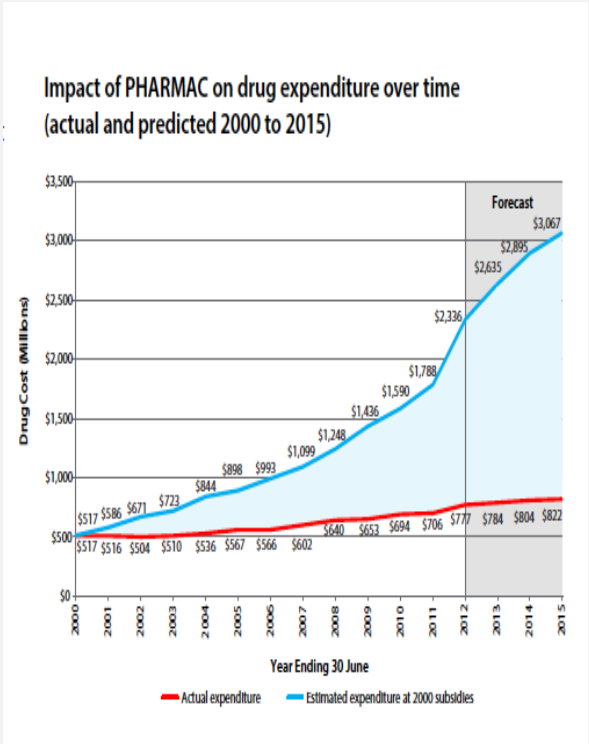
116. To create greater certainty regarding overall expenditure options include fixing a budget and growth rate for reimbursed medicines, with funding for new medicines predicated on obtaining savings from getting better prices for existing ones. This is essentially the model used by the New Zealand Pharmaceutical Management Agency (PHARMAC).[51] (See **Box 2**). Another possible approach would be to allow demand to drive expenditure but reduce prices across the board by one percentage point for each percentage of expenditure growth in excess of growth in GDP (or other designated measure).

Box 2: About New Zealand's Pharmaceutical Management Agency (PHARMAC)[50]

PHARMAC operates within a fixed budget covering community medicines, hospital medicines and vaccines. It uses a range of commercial purchasing strategies to encourage price competition including:

- **Negotiation:** As funding applicants are competing for funding from a fixed budget, negotiation increases competition between suppliers.
- **Tendering:** For off-patent medicines tendering leads to significant price reductions (in some cases > 90%). The successful tenderer gets sole subsidized supply of the medicine for a fixed term thus creating maximum incentive to offer the best price.
- **Reference pricing:** Under therapeutic reference pricing the same subsidy is applied to medicines with the same or similar therapeutic effect.
- **Rebates:** Contracts with pharmaceutical companies may include confidential rebates to the public purchasers
- **Expenditure caps:** If annual spending exceeds an agreed expenditure cap, the supplier must refund the balance. This is useful where there is uncertainty around likely uptake of a medicine.
- **Multi-product** agreements (bundling): Suppliers with large portfolios of products may offer price reductions on older medicines in return for a new medicine being subsidized.

The impact of these strategies on containment of drug expenditure over time can be seen in the figure opposite.



50 Constitutional Court Case № 5/2014 г.,29 January 2015 г.

51 http://www.pharmac.health.nz/assets/factsheet-01-introduction-to-pharmac.pdf

4. Conclusions

117. This report presents a large number of recommendations and options for the Bulgarian Government to consider. Some of these will be controversial and their feasibility will be subject to influences that may lie outside the health care system. Moreover, no suite of policies, however carefully framed, can satisfy the often-conflicting priorities and needs of all stakeholders. Competitive tendering for off-patent medicines and limiting the brands included on the PDL are likely to meet with resistance from both industry (generic and research-based) sectors; patients may claim it reduces choice, while providers may argue that it interferes with the independent exercise of their clinical judgment and prevents them from taking the best care of their patients.

118. For these reasons the development of an overarching national medicines policy, with priorities and objectives agreed by stakeholders, should be a key priority. Getting stakeholders to agree and commit to supporting an explicit set of policy objectives is crucial to successfully implementing reforms that, while consistent with those objectives, may well be unpalatable to them.

119. Resource constraints will always preclude the subsidy of all effective medicines for all potential patients, and even highly cost effective medicines may be unaffordable if the scale of treatment is large. Insofar as some degree of rationing is inevitable, those responsible for making the decisions must ensure that the decisions are transparent, publicly accountable, and arrived at only after a thoughtful assessment of the clinical and economic evidence, undertaken by competent and disinterested experts, and having regard to societal values and priorities, wherever possible.