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# Evidence-based decision making in healthcare in Central Eastern Europe

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## The Fourth International Conference: Evidence Based Decision-Making in Central Eastern Europe Health Care

Belgrade, Serbia, 15–16 May 2014

The Pharmacoeconomics Section of the Pharmaceutical Association of Serbia organized a 2-day international conference on decision making in healthcare in Central and Eastern Europe with a focus on reimbursement decisions for medicines using health technology assessment (HTA) [1]. The aim of this conference was to showcase best practice examples in pricing and reimbursement decision making in Europe and also discuss common challenges and possible ways to overcome them, present new pharmacoeconomic methodologies and outcomes research techniques and learn about the latest trends in health economics modeling. Speakers included international and local experts in pricing and reimbursement decisions representing different stakeholder groups.

### Background

Obtaining value for money and ensuring the long-term sustainability of healthcare systems is a priority in all European countries and beyond. Achieving these objectives becomes even more important for countries with comparatively less resources available to spend on healthcare like Central and Eastern European (CEE) countries. However, they also face the greatest challenges in pursuing these objectives due to a number of factors. Some of these factors are related to the country's health and political system and include limited capacity to introduce economic principles in health care decision making, greater impact of political interference and government changes on health care decisions and governance, dominance of budget imperatives over cost-effectiveness criteria and developing healthcare systems. Another important factor relates to the financial attractiveness of these markets in terms of size and affordability. The modest population size and low spending on health pharmaceuticals in many CEE countries could result in limited attractiveness of their markets to pharmaceutical companies launching new high-cost therapies. The latter, unwilling to deviate too much from average official prices, may also be reluctant to offer the same

confidential pricing conditions offered to larger Western European countries.

Drawing from the wide-ranging experience of CEE and beyond, a faculty of international experts in health care decision making presented examples of instrument for evidence-based decision making, challenges hampering their implementation and suggested possible ways to overcome them.

### Health care decision making

Using the example of the Polish Pricing Authority, Krzysztof Łanda (CEO HTA Audit, Poland) showed how it is possible to reduce waiting times by regulating tariffs of health services. While the regulation of non-drug tariffs remains a challenge in Poland, the improvement of the drug pricing policy, following the introduction of the Pricing Authority in 2011, enabled €477.8 million and €215 million savings on drugs in 2012 and 2013, respectively (HTA Audit's estimations based on databases from National Health Fund website). The role of the Polish Economic Commission was then compared with the Australian Independent Hospital Pricing Authority, which is tasked with setting the national efficient price for Australian public hospital services. The national efficient price is

calculated using a cost model based on cost and activity data from three previous years. This is then converted into a pricing model using national weighted activity unit and is a major determinant of government funding for public hospital services serving as a benchmark for efficient cost [2].

Mark Parker (Senior Economic Modeler at the University of Liverpool, UK) provided an overview of health economics-based instruments that can be used to guide decision making. These include budget impact analysis (BIA), cost-effectiveness analysis, multiple criteria decision analysis and value-based pricing. Independent of the instrument used, transparent decision-making criteria are a necessity, but not sufficient prerequisite for decisions to be politically acceptable.

### Evidence tools in decision making

When considering a technology for reimbursement, cost-effectiveness analysis tells us what the incremental cost for an additional unit of benefit of the new technology is in comparison to current available treatments (although the analysis can also compare two established technologies). However, it does not tell us what the total cost of treating the eligible patient population is. Information on the actual budget impact of accepting a new drug for reimbursement is crucial because even if a drug is cost-effective, it may not be affordable without significant changes in budget allocation. In Poland, BIA is required when introducing or increasing the price of an innovative or generic drug. Using concrete examples from her own work, Daria Szmurlo (Senior Health Economist and Team Leader at HTA Consulting) showed wide range of applications BIA can have in supporting decision making. These include forecasting the reimbursement cost of new technologies, developing risk sharing schemes (RSS), creating therapeutic reference price groups, negotiating prices and predicting impact of policy changes. BIA can be conducted from different perspectives, thus becoming a useful instrument not only for public payers but also for service providers, pharmaceutical companies and decision makers.

Using Croatia as an example, Vanesa Benkovic (Senior HTA and Health Research Consultant at Solpharm) discussed some of the challenges hampering access to innovative drugs in CEE. These can be ascribed to challenges relating to the decision-making process, including political interference in resource allocation, predominant role of budget impact consideration, limited transparency, accountability and capacity to conduct HTA. In addition, there are also financial challenges including debt accumulation by healthcare providers, reimbursement delays and restricted budget available for drugs. This translates into limited breadth and depth of the benefit package and higher out-of-pocket spending on individuals. Existing challenges have been exacerbated by the financial crisis and the need to comply with the Maastricht criteria of maximum debt levels, heavy reliance on hospital care and an ageing population. In response to these challenges, health authorities have introduced coping mechanisms, including long waiting times, limiting reimbursement indications, requiring failure of other treatments before access is granted, engagement in RSS with the manufacturer

but also simply shifting the financial risk to the individual. The speaker concluded with calling for partnerships, rather than competition, between the public sector, the pharmaceutical industry, patients and professionals as the way forward.

Similar challenges were highlighted to affect access to innovative medicines in Bosnia and Herzegovina (BH) by Tarik Catic (Founder and President of ISPOR BH). As recognized by the previous speaker, the impact of these factors is amplified for orphan drugs. However, while Croatia has a special fund for expensive drugs including orphan drugs, no special funding arrangements or RSS are available for orphan drugs in BH. While not yet implemented, the legal basis for patient registries is available. Further, recent developments such as the introduction of e-healthcare IDs in the Canton of Sarajevo, the diabetes registry led by ISPOR BH and the renal registry of the Society for Nephrology, Dialysis and Transplantation in Bosnia [3] could pave the way for their implementation. Registries expansion would create new opportunities to engage in RSS and, therefore, serve as tool to improve access to patients.

Building on the potential of patient registries, Tanja Novakovic (President of the Pharmacoeconomic Section of the Serbian Pharmacist Association) discussed the use of big data to support decision making. The digitization of patient data provides an unprecedented opportunity to complement data from randomised clinical trials (RCTs) and provide insights into effectiveness, costs and safety in real life, based on large patient populations. 'Big data' represent a collection of data sets that is difficult to process with conventional analytical tools (e.g., Excel, Stata, SPSS, etc.). However, due to their high volume, high velocity and high variety [4], a number of challenges need to be addressed. These include storage and analytical capacity as well as privacy protection before they can be converted into knowledge that can be used for decision making. Concrete steps have already been undertaken to address these issues with new storage systems and analytical software launched in recent years that have enabled researchers to use these data for analysis [5]. A practical application of the use of big data in discrete event simulation [6] for HTA was explored during a workshop led by Mark Parker.

### Clinical data in decision making

Clinical data is key to evidence-based decision making and there are different ways in which it can be used. In his presentation, Janko Samardzic (Specialist in Clinical Pharmacology at the Institute of Pharmacology and Toxicology, Serbia) discussed the role of prescription guidelines in improving rational prescribing. A survey in 2009 found that in 23 of the 27 EU Member States, payers had introduced prescription guidelines and in nine Member States these guidelines were obligatory [7]. The impact of prescription guidelines is greatest when implemented together with measures such as monitoring e-prescribing and e-guideline systems, both of which are expected to be implemented in Serbia soon.

Eldon Spackman (Research Fellow at the University of York, UK) discussed the use of off-label comparators in HTA based on the experience of the National Institute for Health and Care

Excellence (NICE). Although NICE is not able to recommend use of off-label comparators, their inclusion as a comparator in HTA is allowed, if justified. Out of 54 single technology appraisals completed between 2010 and 2012, scopes of 14 appraisals recommended the inclusion of at least one off-label comparator [8]. Using the example of bevacizumab in England, the presenter showed how lack of incentive on the manufacturer's side to apply for a license may result in nonoptimal outcomes. Bevacizumab, a drug approved for cancer, was found to be equally effective [9] to ranibizumab for the treatment of wet age-related macular degeneration; however, because it is not approved for this indication, NICE could not recommend its use. It was estimated that the National Health Service could save GBP 84.5 million annually based on injecting 17,295 eyes each year by switching from ranibizumab to bevacizumab [10].

### Best practices in decision making

This session included an overview of pharmaceutical policies to manage the introduction of new drugs and improve rational use, recent changes in HTA systems in Germany and Romania and options to introduce HTA in Serbia.

In the past years, a number of new drugs have been launched at very high prices, yet, bringing modest healthcare gains [11] to the extent that some believe most new drugs and indications provide minor or similar health improvements to existing therapies [12]. Using the example of dabigatran [13], Brian Godman (Senior Researcher at the Karolinska Institute, Sweden and Professor Strathclyde Institute of Pharmacy and Biomedical Sciences, Scotland) presented the model of pre-, peri- and postlaunch activities [14] to optimize use of new drugs. The model starts from horizon scanning and goes all the way to evaluating adherence to guidelines. Further, he presented evidence of ongoing measures to release valuable resources from greater use of generics. Examples include the preference pricing policies in the Netherlands [15], which led to low prices for generics such as omeprazole; a package of generic-friendly policies introduced in Lithuania [16] and the Republic of Srpska [17] showing that good policies rather than population size are key to achieving low prices for generics; and a set of demand-side measures encompassing education, engineering, economics and enforcement (the '4Es') exemplified by the Wise List in Stockholm [18]. According to the speaker, continuous cross-countries learning to improve the rational use of medicines building on examples such as the Wise List in Stockholm will be essential to sustain progress made toward universal health coverage.

In 2011, Germany introduced a system of early value assessment (Act on the Reform of the Market for Medical Products [AMNOG] [19]) moving away from a system of relative free pricing with volume controls and some statutory rebates and contractual discounts. While the latter have been maintained and their absolute value and share of sales have increased over time, evidence on the added therapeutic benefit of new drugs, rated on a 1 to 6 scale similar to the French Amélioration du Service Médical Rendu/Improvement (ASMR)

system, is now used in pricing negotiations. Examples from the first 74 assessments conducted under this new system were presented by York Zöllner (Professor of Health Economics at Hamburg University of Applied Sciences). These suggest that robust evidence and well-designed trials are rewarded in terms of price, while for instance the lack of comparator arm, poor quality RCT design and use of an off-label comparator have penalized drugs under assessment. Under AMNOG arrangements, drugs with no additional therapeutic benefit are clustered in a reference price group. Currently, 78% of all drugs on the German market fall under reference pricing.

Alin Liviu Preda (ISPOR Romania) presented the difficult process of introducing HTA in Romania amid government changes, involvement of different external advisors [20–22], lack of consensus among key stakeholders and sudden policy changes such as recent withdrawal of a previously approved HTA methodology. This methodology was based on a simple scorecard system with a 10-point scale and a 6-point threshold for a positive decision. The scoring system was meant to account for decisions made by HTA bodies in France and the UK, the reimbursement status in other EU countries, relative efficacy/effectiveness, safety and patient-reported outcomes. He concluded by highlighting the need for a comprehensive approach to HTA including health financing and the definition of the basic health care package, a clear and realistic implementation strategy and a 'change champion' in the government who will engage in this process with a long-term mandate.

Similarly to Romania and other CEE countries, Serbia is trying to strengthen the role of pharmacoeconomics in its decision-making process for drug reimbursement. To fill the interim gap while developing national capacity to conduct HTA, Ruth Lopert (Adjunct Professor, George Washington University) proposed the introduction of a price benchmarking system based on the outcome of HTA appraisals in countries with well-established HTA systems, known prices and appraisals results. This mechanism assumes a fixed relationship between cost-effectiveness and gross domestic product per capita, the latter used as a proxy for affordability. Under this assumption, a drug is unlikely to be cost-effective if listing is consistent with the conditions considered cost-effective in the reference country and the price is higher than the reference country price adjusted for relative per capita gross domestic product. However, she also stressed that the result is indicative only, and the process is not a substitute for properly conducted HTA, but could be applied as a 'quick check' of value-for-money of current (and proposed) drugs only, and as a guide to price negotiation.

### Decision making in Serbia

Dragana Baltezarević (Republic Health Insurance Fund, Serbia) provided an overview of the pricing and reimbursement process in Serbia. Assuring quality of generics, improving rational use of medicines, finding sustainable procurement mechanisms for essential medicines, controlling costs through increased use of economic principles in the decision-making process, conducting more analysis of drug utilization including cross-country

comparisons and more reliable budget impact forecasts that could be used to conclude volume cap agreements for new medicines were identified as some of the main challenges and aspiration currently faced in Serbia. Recent developments like the introduction of a legal basis to implement RSS and volume cap schemes provide opportunities to address some of these issues together with participation in international networks such as the Pharmaceutical Pricing and Reimbursement Information [23] and Piperska [24]. Future priorities for Serbia include developing a national pharmaceutical policy, the definition of a high threshold value for innovative medicines, introducing electronic file submission for reimbursement applications and central procurement for pharmacies, establishing an HTA unit and building national capacity in economic evaluation, greater collaboration with other countries on drug utilization and starting to implement RSS.

While the focus of this conference was on decision making in the pharmaceutical sector, recent reforms are also trying to improve provider payment mechanisms. Predrag Djukic (Delivery of Improved Local Services [DILS] Project, Ministry of Health, Serbia) discussed current efforts to introduce diagnostic-related groups for inpatient acute care services in the country. Their introduction is initially planned for reporting and analytical purposes with the idea to then gradually move toward their implementation as a payment mechanism.

Bojan Trkulja (Managing Director of the Innovative Drugs Manufacturers' Association, Serbia) called for a switch from a cost-containment attitude based on price cuts, de-listings, international reference pricing, generic promotion through INN tendering and substitution, reimbursement restrictions to an approach based on value-based pricing, risk sharing agreements, use of health economic evaluation and evidence-based decisions.

## Conclusions

Despite the diversity of the countries represented and issues portrayed, various common themes emerged: the limited number of new chemical entities accepted for reimbursement in the CEE, delayed access, cost-shifting to patients and limited funding for orphan drugs. Beyond the health system itself, health system governance was recognized as being deeply affected by political priorities and changes in government.

It was also clear that speakers had diverging opinions on the value of new medicines with some presenting figures showing

that life expectancy increased at a higher pace between 2000–2009 in countries where new drugs have been on the market for more years [25], while others highlighting the modest survival gains brought by new drugs at very high prices [12]. While the contribution of new medicines such as antibiotics, vaccines, insulin and other basic medicines for diabetes and cardiovascular conditions to population health in the last century is unquestionable, there is evidence from regulatory and HTA assessments that survival gains for cancer drugs are mostly very modest. For example, only 3 of the 12 cancer drugs approved by the US FDA in 2012 actually prolonged survival and two of them by less than 2 months [11]. Further, studies looking at the overall impact of novel medicines on survival should be interpreted with caution due to methodological challenges in conducting this type of analyses [26]. Due to differences in demography, burden of disease, clinical practice, resource use and unit costs just to name a few, caution is also needed when transferring results of HTA from one country to another [27–29] and adjustments need to be made before using results from other countries to make resource allocation decisions in other settings [30].

Of course, there are also other important outcomes to evaluate such as symptomatic improvements, whether a new drug enables the patient to go back to work and/or significantly increases their quality of life. In this respect, HTA plays a vital role in assessing the additional benefits of new drugs in comparison to available treatments and comparing these with their additional costs. However, because medicines are only one component of disease therapy, to achieve better health outcomes, it is also essential to strengthen other component of the healthcare systems, particularly early diagnosis and access to quality health care services. Only a strong and resilient health care system will ultimately be able to deliver good outcomes for patients, and medicines are only one component of it.

## Financial & competing interests disclosure

*The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.*

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