As part of Minister of Health and Social Welfare Darko Milinović’s overall health care reform, in 2009 and 2010 Croatia substantially reformed its pricing and reimbursement regulation for medicines. The main goals of the reform were to (a) maximise value for tax payers’ money, (b) improve efficiency and transparency in high level decision making, and (c) ensure ethical medicines promotion practices. The results of the reform enabled the Croatian national health insurance fund (Croatian Institute for Health Insurance – HZZO) to generate extensive savings, while at the same time improving access to innovative medicines.

In 2009, HZZO expenditure on prescription medicines amounted to 2.9 billion Kune (kn) (€393 million)*, with an additional 2 billion kn (€271 million) spent on hospital medicines, of which HRK480 million (€65 million) went on expensive products funded from a budget separate to that for regular hospital expenditure. Due to the introduction of modest co-payments (15kn or €2 per prescription) and reference pricing, HZZO expenditure on prescription medicines decreased by 2.9% in comparison with 2008.1

In the twelve month period from July 2009 to July 2010 as many as 47 innovative molecules were added to the different HZZO lists of reimbursed medicines and thirteen innovative molecules to its list of expensive hospital medicines. For comparison, a total of 45 products were listed in the period from 2002 to 2009. Comparing expenditure in the first six months of 2009 and 2010, HZZO expenditure on prescription medicines decreased by an additional 13% from 1.7 to 1.5 billion kn (€230.5 to €203.4 million), while its expenditure on expensive hospital medicines decreased by 28.5% from 219 to 157 million kn (€30 to €21 million). Total savings generated by the reform across the two periods amounts to 295 million kn (€40 million), a 22% reduction.2

So what did the reforms involve? We now summarise the pricing and reimbursement system in Croatia along with the major changes introduced by the reform.

Summary: In 2009/2010, Croatia substantially reformed its pricing and reimbursement regulation of medicines with the aims of maximising value for invested funds, increasing efficiency and transparency in high level decision making, as well as ensuring ethical pharmaceutical marketing practices. Most notably, the reform measures included: clearly defined judgment criteria and full public disclosure of the reimbursement decision-making process; pricing reforms; strengthening of evidence-based medicine and health economic requirements for submissions; payback, rebate and cross-product agreements; and mandatory reporting of promotional expenses and all financial transactions between pharmaceutical companies and doctors employed by the public health care system.

Key words: Pricing, reimbursement, medicines, transparency, value for money

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* One Croatian kuna equals €0.135

The pharmaceutical pricing and reimbursement system

The HZZO holds a virtual monopoly on pricing and reimbursement in the markets for prescription and hospital medicines. Only HZZO contracted hospitals and primary care physicians can prescribe medicines that are paid by mandatory health insurance. The HZZO implements two lists: the ‘basic’ list with all essential medicines covered by mandatory insurance, and the ‘complementary’ list with medicines covered partially through mandatory insurance and partially by out-of-pocket payments. Applications for reimbursement are submitted to the HZZO Committee for Medicines for consideration. The committee delivers a non-binding opinion on all applications to the HZZO management board, which makes the final decision.

In Croatia, international price comparisons are used for setting maximum wholesale prices (Table 1). The system takes into account drug prices in Italy, France and Slovenia. Prices in Spain and the Czech Republic are consulted if data from Italy, France and Slovenia are not available.

The HZZO also sets reimbursement limits for most prescription medicines through annual internal reference pricing. Forty-one clusters are formed at Anatomical Therapeutic Chemical Classification

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Table 1: HZZO international price comparison mechanism for setting maximum wholesale prices

<table>
<thead>
<tr>
<th>Listed drugs determined through annual price recalculations</th>
<th>New drugs introduced to lists</th>
</tr>
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<tbody>
<tr>
<td>Drugs protected under patent in Croatia or any EU member state: up to 90% of the average price in Italy, France and Slovenia.</td>
<td>Original breakthrough products: up to 100% of the average price in Italy, France and Slovenia.</td>
</tr>
<tr>
<td>Drugs not under patent in Croatia or any EU member state: up to 65% of the average price in Italy, France and Slovenia.</td>
<td>Original ‘me-too’ products: up to 90% of the average price of equivalent drugs in Croatia.</td>
</tr>
<tr>
<td>Generic products: up to 70% of the average price in Italy, France and Slovenia and up to 90% of the price of the last bioequivalent generic introduced to the list.</td>
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( discredit 3, 4 and 5 using the Defined Daily Dose (DDD) approach. Payment is only granted up to the level of the reference price, while the difference with the actual market price has to be paid by the patient if the company does not accept the reference price (the B list). Companies may opt to negotiate a higher price than the one determined through the reference pricing mechanism, but are obliged to generate equivalent savings to the HZZO through price decreases on other products or through rebate agreements.

The reform: improved decision making and transparency

Two ordinances that regulate the market introduced most of the reform measures: one ordinance established the criteria for wholesale pricing and reporting of the wholesale prices of medicines and a second ordinance established the criteria for inclusion of medicines in the basic and supplementary reimbursement lists of the HZZO.

As a result of the reform, applications for the inclusion of productions on any of the HZZO lists are now published on the HZZO web page (http://www.hzozo-net.hr) within five working days of receipt. The information includes the identity of the applicant, the date of application receipt and the subject of the application. The list of HZZO Committee for Medicinal Products members with short CVs, as well as the dates and agendas of committee sessions, are also published online.

Improvements have been made in the committee’s methodology for making recommendations and transparency has been increased. The committee now operates in two semi-annual cycles. The cycles consist of four regular sessions where the committee discusses submitted applications and a fifth regular session where it ranks the applications in terms of those that may increase HZZO drug expenditure. Ranking is undertaken using a Delphi process – a consensus building method ensuring that all members of the committee carry equal weight in the decision-making process.

In addition, the new ordinances introduced detailed criteria on which the committee must base their recommendations. These include: (a) the product’s importance from the public health perspective; (b) its therapeutic importance; (c) its relative therapeutic value; (d) an assessment of ethical aspects; and (e) the quality and reliability of data and assessments from reference sources. For example, with regard to relative therapeutic value, a product may be classified in one of three groups:

1. A product with new therapeutic value, when it concerns a medicinal product for treatment or prevention of diseases, conditions or disorders with no currently available effective treatment.
2. A product with added therapeutic value, when, compared to a standard or typical medicinal product or treatment, it refers to:
   - more favourable effect on final treatment results,
   - more favourable effect on substitute treatment results,
   - more favourable effect on quality of life,
   - efficient treatment of disease symptoms,
   - improved safety profile of a medicinal product,
   - a more patient-friendly use of a medicinal product,
3. A product without proof of new or added therapeutic value.

Furthermore, there are increased requirements in the application which the committee assesses. Most importantly, these include having a tabular presentation of the status of the product in respect of health insurance or health care systems of all Member States of the European Union and, if available, a decision or opinion about financing of the product issued by the competent authority engaged in health technology assessment. Information should also be presented on indications and instructions for use, the amount covered by compulsory health insurance, any surcharges and other information relevant to the financing of the medicinal product in individual Member States. Scientific evidence must also be presented demonstrating the advantages of the medicinal product for suggested indication(s) over comparator treatments, primarily over medicinal products already included in the basic or supplementary reimbursement lists of the Institute. Meta analyses and systematic appraisals should be presented where available.

The therapeutic guidelines of both Croatian and European expert associations for indications for which an application has been submitted will be taken into account. A description of current clinical practice in Croatia by indication for which the application has been submitted and for which the medicinal products already included in the Institute’s lists are used, must be provided along with comments on efficacy and safety, and a table comparing the relative price of treatment. There is also a requirement for a description and analysis of the effect of the use of the new pharmacological therapy on patient health care resulting from the inclusion of the medicinal product on the list (including the use of complementary products and services). An estimate of the number of patients likely to receive the product over a three-year period is also required, as well as an estimate of the proportion of patients who could only be satisfactorily treated with the new medicinal product, compared to those satisfactorily treated with products already on the Institute’s approved lists.

Criteria for the inclusion of products in the HZZO list of expensive products have also been defined. These include a need to show...
that use of the product represents a break-through in the risk-benefit ratio of treatment for a given indication, in comparison with medicinal products already included in the basic reimbursement list of the Institute. The product must be intended for hospital use and not subject to medical prescription. Both guidelines for prescription, as well as the clinical pathway for the condition for which the medicinal product is to used, must be strictly defined by the Croatian Medical Association. There must be no generic equivalent or the product must be on the European Commission Register of Designated Orphan Medicinal Products. In terms of cost, a budget impact analysis must demonstrate that use of the product could not be financed through routine hospital budgets because of the very high treatment costs. It should also be noted if products with similar therapeutic and pharmacological properties, but higher therapy costs, are already included in the list of expensive medicinal products.

One additional change introduced as part of the reforms means that when a company now wishes to appeal against a decision made by the HZZO management board on the listing of a medicinal product, the case must proceed to court, unlike the situation previously where arbitration procedures were used.

### Ensuring value for tax payers’ money

All applications for reimbursement have to be accompanied by budget impact analyses. These are undertaken according to strict criteria that largely adhere to ISPOR (International Society for Pharmacoeconomics and Outcomes Research) principles of good practice for budget impact analysis.

The financing of ‘expensive products’ is now regulated by payback agreements concluded between the marketing authorisation holder and the HZZO. The HZZO finances the treatment of a precisely defined number of insurants (based on the results of the budget impact analysis), while the marketing authorisation holder ensures the supply of its medicinal product to additional insurants (if needed) at its own cost through donations or pays back the overspend to the HZZO. Prices can also be determined using a cascading approach with regard to the number of insurants receiving the medicinal product.

When concluding the agreement, the HZZO takes into account the total consumption of all medicinal products for the given therapeutic indication. This can translate to disease-wide agreements for all market authorisation holders with medicinal products for a particular condition. The new byelaws also introduce cross product agreements. Applicants are allowed to submit binding offers where the application, which refers to the product considered by the Committee for Medicinal Products, is connected with a parallel proposal for the reduction in the price of the medicinal product already included in the Institute’s basic reimbursement list. In this way new drugs are added to HZZO lists without additional costs, as the costs borne by the introduction of new products are offset through savings achieved by price reductions in products that are already reimbursed.

Furthermore, internal reference pricing is now better regulated. Groups are formed at the third or higher ATC levels. Reference prices are determined (to a large extent by taking account of the price by DDD) by unit dosage form for the same or similar pharmaceutical forms for each strength level of the active substance and each pack size separately. Reference prices are determined on the basis of the lowest price of a product which recorded at least 5% of sales within a therapeutic group over a twelve month period preceding the reference pricing process. This principle was adopted to avoid the possibility of market shortages.

### Ethics

All applicants to the lists are obliged to enter into a uniform agreement on the ethical promotion of medicines. This entails substantial financial penalties for unethical promotion. The main features of the agreement are shown in the panel above.

All features of the agreement apply to third persons working on behalf of the marketing authorisation holder. A financial revolving deposit mechanism has now been put in place to guarantee implementation. Companies are obliged to deposit their promotional budgets (estimated in the first year of agreement implementation at a minimum of 3% of annual revenue from the HZZO) to the HZZO in quarterly instalments and present all promotion based expenses, including all payments to individuals employed in the public system, quarterly. Payback of the funds in question is also delivered quarterly.

Penalties for unethical promotion include delisting, informing the general population of unethical behaviour and withdrawal (in part or total) of the quarterly deposit. The HZZO Committee for Medicinal Products then functions as the arbiter ensuring the implementation of the agreement, while the management board takes any final decision on any punishments and penalties to be incurred.

### Key features of uniform agreement on the ethical promotion of medicines

- Mandatory reporting of all promotional expenses and financial transactions between companies and doctors employed by the public health care system.
- Ban on advertising and distribution of prescription drugs to the general population.
- Ban on informing the general population of ongoing applications to avoid unethical pressure on the HZZO Committee for Medicinal Products.
- Ban on promotion targeted at doctors based on information that has not been scientifically proven.
- Ban on financial remuneration or remuneration of any kind to doctors for prescribing.
- All promotional events have to be educational and professional. They may not include more than 25% of time for unprofessional activities.
- Companies must provide detailed information to the HZZO of any organised promotional events 15 days in advance.
- The HZZO has to be notified of all clinical studies, including post marketing surveys.
- Representation costs are limited to 1,000 kn (€ 135) per doctor (does not include education).
- Individual sales representatives are allowed 15 minutes contact time per doctor per month.

### References

