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Availability and affordability of medicines and assessment of quality systems for prescription of medicines in the Republic of Moldova: final report

Report

Original citation:

Sautenkova, Nina, Ferrario, Alessandra, Bolokhovets, Ganna and Kanavos, Panos (2012) *Availability and affordability of medicines and assessment of quality systems for prescription of medicines in the Republic of Moldova: final report*. Health policy paper series, no. 6. World Health Organization, Regional Office for Europe, Copenhagen, Denmark.

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Originally available from [World Health Organization, Regional Office for Europe](#)

Available in LSE Research Online: May 2013

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World Health
Organization

REGIONAL OFFICE FOR

Europe

Republic of Moldova

Health Policy Paper Series No. 6



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AVAILABILITY AND AFFORDABILITY OF MEDICINES AND ASSESSMENT OF QUALITY SYSTEMS FOR PRESCRIPTION OF MEDICINES IN THE REPUBLIC OF MOLDOVA



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FINAL REPORT

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Keywords

DRUG COSTS

DRUG INDUSTRY – STANDARDS

ECONOMICS, PHARMACEUTICAL

PHARMACEUTICALS AND BIOLOGICALS

QUALITY CONTROL

REPUBLIC OF MOLDOVA

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Abstract

An overall assessment of the pharmaceutical sector in the Republic of Moldova was performed during 2011–2012, with the purpose of providing the Ministry of Health with comprehensive evidence regarding access to essential medicines of good quality. This report presents the results, based on a secondary analysis of evidence collected during a series of assessments conducted by the World Health Organization Regional Office for Europe in collaboration with the Ministry of Health of the Republic of Moldova, the Medicines Agency, Nicolae Testemitanu Republic of Moldova State Medical and Pharmaceutical University, and Health Action International. The assessments covered the areas of: public procurement; main regulatory functions; availability, affordability, prices and price components of essential medicines; and an evaluation of the essential list of medicines, prescribing practices and pricing policies. The main recommendations of the report provide insights into ways of improving regulatory and procurement practices, along with the best methods to constrain the costs of medicines.

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Acknowledgements

The authors gratefully acknowledge the input of a significant number of experts and stakeholders who took part in four studies in 2011, which formed the basis for this report.

The publication forms part of the Health Policy Papers series launched in 2011 with the aim of strengthening the health system in the Republic of Moldova in line with the national health policy and strategy for the development of the health care system. It has been prepared under the guidance of Mr Andrei Usatii, Minister of Health of the Republic of Moldova and Jarno Habicht, representative of the World Health Organization (WHO).

Special thanks are owed to the Ministry of Health of the Republic of Moldova for its invaluable contributions to the development of the pharmaceutical sector and its support of the work.

Particular thanks are given to Rita Seicas for her continuous input in the drafting of the report and facilitating the work of the local team, as well as to Mihail Lupu, Lucia Turcan and colleagues from the Medicines Agency in the Republic of Moldova for supporting the logistics, facilitating the meetings with stakeholders and providing valuable insights into the operation of the Moldovan pharmaceutical sector.

The work of WHO consultants Margaret Ewen, Zinaida Bezverhni, Vladimir Safta, Henk den Besten, Kristin Raudsepp and Ilze Aizsilniece is also acknowledged.

This document expresses the authors' personal views and opinions, which do not necessarily reflect the views of the institutions they are affiliated with.

This report contributes to the Biennial Collaborative Agreement 2012–2013 between the Ministry of Health of the Republic of Moldova and the WHO Regional Office for Europe.

This document has been produced with the financial assistance of the European Union within the technical assistance programme coordinated by WHO. The views expressed herein can in no way be taken to reflect the official opinion of the European Union.

Abbreviations

| | |
|-----|------------------------------------|
| ATC | anatomic therapeutic chemical |
| CI | confidence interval |
| GMP | good manufacturing practices |
| INN | international non-proprietary name |
| IR | incidence rate |
| MPR | median price ratio |
| OR | odds ratio |
| PS | procurement and supply |
| WHO | World Health Organization |

Objectives of this study

The purpose of this study is to provide the Ministry of Health with comprehensive evidence regarding the availability and affordability of good quality essential medicines in the Republic of Moldova.

The study looks at:

- the possible barriers to the availability and affordability of essential medicines;
- the level of prescription medicine prices in the Republic of Moldova in comparison with other countries;
- the prevailing prescribing practices with regards to generic and brand medicines;
- the extent to which the Moldovan authorities spend public funds on medicines which are most needed for the local population, in other words whether scarce resources are allocated optimally;
- the components of medicine prices and tries to identify where in the procurement and supply (PS) chain there may be opportunities for improvements with regard to distribution; and
- whether through robust regulatory practices it is ensured that only medicines of the highest quality are available on the market.

The report is structured as follows:

- background to the organization and financing of health care;
- methodology used to compile the material;
- results regarding access to medicines, PS and the rational use of medicines;
- discussion of the key points formulated above;
- conclusions and recommendations regarding issues identified in the pharmaceutical system.

Background

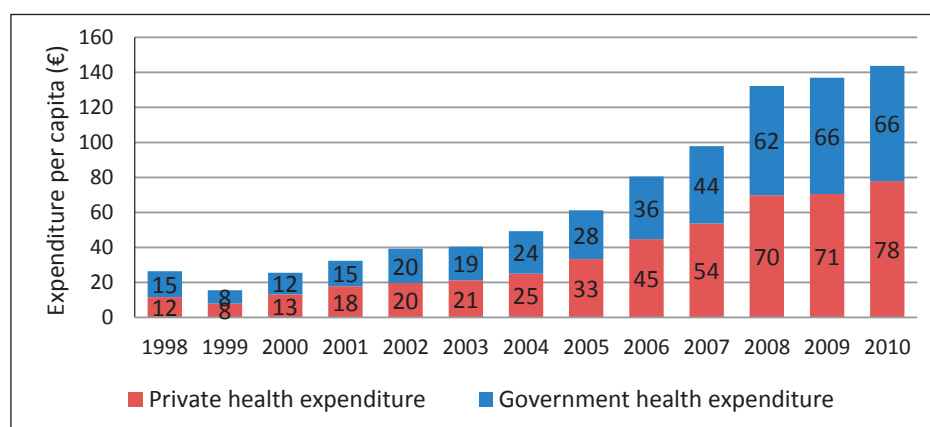
Population, health and epidemiology statistics: an overview

In 2012, the total population of the Republic of Moldova was 3 559 500 (excluding the population on the left bank of the river Nistru and the town of Bender (Transnistria)). This was 5000 less than in 2011 and predominantly rural (urban to rural ratio: 0.72) (1). In 2010, gross domestic product (GDP) was €4383 million, corresponding to a GDP per capita of €1231 (at 2012 exchange rates) (2).

In 2010, life expectancy at birth was 65 years for men and 73 years for women (1). In the same year, the infant mortality rate for children aged under 1 year was 16 per 1000 live births (3). For children under the age of 5 years, the mortality rate was 19 per 1000 live births in 2010 (3). The maternal mortality ratio was 41 per 100 000 live births in 2010(3).

Total health expenditure increased from €26.5 per capita in 1998 to €143.7 per capita in 2010 (at current exchange rates) (Fig. 1). Between 1998 and 1999, there was a decrease in total health expenditure owing to the negative effect of the Russian crisis in the Republic of Moldova. Since 2000, however, total health expenditure has increased gradually from €25.5 per capita to €61 per capita in 2005 and €144 per capita in 2010. This remains far below the European average of €1585 per capita (2009 figures).

Fig. 1. Total health expenditure per capita, 1998–2010



Source: WHO Global health expenditure database (4).

The proportion of total private spending has remained high, accounting for 54% of total health expenditure in 2010. More than half of out-of-pocket expenditure on health (70% in 2008, 73% in 2009 and 72% in 2010) was related to pharmaceuticals (4). The latest available data (2010) show that 83% of total private expenditure on health came from out-of-pocket sources, with the remainder coming from private health insurance. External sources of health care funding, such as international aid, play an important role, amounting to almost 10% of total health expenditure in 2010.¹

In 2009, a WHO PS assessment mission to the Republic of Moldova estimated total pharmaceutical expenditure to be €126 million (unpublished data), compared with €69 million in 2005 (6). Pharmaceutical expenditure grew at an average rate of 8% per year between 2000 and 2005 (6) and 11% between 2005 and 2009.

The 2009 estimate of €126 million includes €11 million of locally produced and consumed pharmaceutical products (an additional €6 million of locally manufactured products is exported). The same assessment found that overall more than 91% (by value) of the medicines consumed in the country are imported (unpublished observations). Of total pharmaceutical spending, €25 million was publicly and €101 million was privately funded.

¹ In comparison to government and private expenditure as percentages of total health expenditure, which refer to financing agents, this indicator refers to the origin of the resources used to buy health services. Some of these external sources are channelled through the government budget, some through insurance agencies and some through the private sector or nongovernmental organizations. As such, these funds cannot simply be added to those reported in the earlier breakdowns (5).

In terms of the disease burden, cardiovascular diseases are the main cause of mortality (66.3 deaths per 10 000 population), followed by cancer (16.1 deaths per 10 000 population) and diseases of the digestive system (9.7 deaths per 10 000 population). Respiratory diseases (incidence rate (IR): 133.8 per 10 000 population) were the main cause of morbidity followed by trauma and poisoning (IR: 44.4) and infectious and parasitic diseases (IR: 30.1) (Table 1).

Table 1. Leading causes of mortality and morbidity, Republic of Moldova, 2009

| | Disease | Death rate per year per 10 000 population | Disease | Incidence per year per 10 000 population |
|----|---------------------------------------|---|---|--|
| 1 | Cardiovascular diseases | 66.3 | Respiratory system diseases | 133.8 |
| 2 | Cancer | 16.1 | Trauma and poisoning | 44.4 |
| 3 | Diseases of the digestive system | 11.6 | Infectious and parasitic diseases | 30.1 |
| 4 | Trauma and poisoning | 9.7 | Skin diseases | 20.7 |
| 5 | Respiratory system diseases | 6.5 | Urogenital diseases | 20.4 |
| 6 | Infectious and parasitic diseases | 2 | Diseases of the digestive system | 19.7 |
| 7 | Nervous system diseases | 0.14 | Cardiovascular diseases | 16.8 |
| 8 | Urogenital diseases | 0.92 | Osteoarticular diseases | 14.7 |
| 9 | Complications in the perinatal period | 0.56 | Complications during pregnancy or birth | 13.4 |
| 10 | Congenital malformations | 0.54 | Eye diseases | 9.4 |

Source: based on data from the National Centre of Health Management (7).

Policy frameworks relating to health

The national health policy was approved in 2007 (8) and an associated implementation plan was prepared in 2008.

The official national medicines policy document was updated in 2002 and the associated implementation plan was updated in 2007. The implementation of pharmaceutical policy is regularly monitored and assessed by the Medicines Agency and the Ministry of Health.

Access to essential medicines/technologies, as part of the fulfilment to the right to health, is recognized in the constitution or national legislation. There are official written guidelines on donations of medicines.

Health insurance

A system of national health insurance was introduced in 2004, financed through the payroll tax (7% of salary, shared equally between the employer (3.5%) and the employee (3.5%)) or a flat-rate lump sum for those who are self-employed (€167, or 2772 lei, in 2011 (9)). The government makes contributions for those registered as unemployed. Vulnerable groups such as children aged under five years, pregnant women and the elderly are exempt from premium contributions, which are fully subsidized by the government.

In principle, health insurance is mandatory. In practice, however, coverage is not universal, mainly because a proportion of the self-employed and those employed in the large primary (mostly agricultural) sector often fail to pay contributions and, therefore, remain uninsured. Despite this, insurance coverage has grown steadily from 66.8%² of the total population in 2004 to 72% in 2009 and to 82% in 2010 (10), which corresponds to 18% of the population being uninsured in 2010. This is in line with findings from a recent study in the country showing that 22% of the people interviewed (N=3760) had no health insurance (11). Factors associated with not being insured (as identified through multivariate analysis) included: being self-employed in agriculture (odds ratio (OR): 27.31, 95% CI: 19.60–38.03 in comparison to employed people), being youth (age 24–34 years OR: 5.04, 95% CI: 3.25–7.81 in comparison to those aged 15–24 years), being unemployed (OR: 4.72, 95% CI: 3.39–6.57 in comparison to employed people), being on a very low income (OR: 1.62, 95% CI: 1.13–2.34 in comparison to those with a very high income), and belonging to the male gender (OR: 2.07, 95% CI: 1.65–2.6 in comparison to females) (11).

The benefit package covers most primary care services, emergency services and inpatient care. There can, however, be long waiting lists for some expensive high-technology diagnostic instruments such as magnetic resonance imaging scans. The exact content of the benefit package is redefined annually based on the available budget (11). In addition, all contracted service providers are required to offer some essential services to everyone regardless of their insurance status (11,12).

² A different source reports 75.7% health insurance coverage in 2004 (6).

Methodology

This report is based on a secondary analysis of evidence collected during a series of missions conducted by the World Health Organization (WHO) Regional Office for Europe in collaboration with the Ministry of Health, the Medicines Agency, State University of Medicine and Pharmacy Nicolae Testemitanu of the Republic of Moldova and Health Action International. The following reports were included in this study:

- medicines prices, availability, and affordability and price components in the Republic of Moldova, 2012 (13);
- PS assessment mission to the Republic of Moldova, 2011 (unpublished report);
- pharmaceutical country profile, 2011 (7);
- medicines regulatory assessment report, 2011 (unpublished report).

Evidence from these reports is complemented by information from peer-reviewed literature (11,14), the latest available health system profile from the WHO Health Systems in Transition series (12), reports of international organizations (8,9,15), and grey literature (10) and insights obtained through interviews with a representative from academia in the country and the Deputy Director of the Medicines Agency.

Drug policy in the Republic of Moldova: evidence about performance

Registration and licensing of medicines

Registration of medicines and inspection of facilities

The Medicines Agency is facing a series of problems related to inspection and registration, which are largely the result of poor implementation of legislation, lack of funding and lack of sufficient human resource capacity to cope with the workload.

First, although there is a bioequivalence requirement in the legislation, this is not being implemented so that the quality of generics remains questionable. The main reason for this is the lack of trained staff and associated guidelines. The plan is for such guidelines to be developed and approved by the end of 2012, using European guidelines on bioequivalence as a model.

Second, there are no legal provisions requiring the publication of a summary of product characteristics of the medicines registered.

Third, temporary and conditional approval is not clearly defined in the legislation, although it is being implemented by the Ministry of Health.

Fourth, pressures from local and foreign manufacturers to register products quickly were reported during a 2011 WHO mission assessing procurement and systems for pharmaceuticals in the country. This causes a conflict of interest in the Medicines Agency, which is tasked to ensure the quality and safety of medicines but, given its involvement in procurement (see section on procurement), also has an incentive to register medicines quickly, particularly low-cost generics so that they can be included in future tenders.

Fifth, there are other conflicts of interest within the Agency which need to be addressed, such as registration of inspectors participating in trials to collect data for marketing authorization applications paid by manufacturers.

Sixth, a registration timeline of 90 days applies to both originator and generic medicines, which is considered unrealistic. A motion was recently put forward in the parliament to extend the registration timeline to up to 210 days for all medicines, whether branded or generics.

Finally, there is limited capacity to inspect all new suppliers both in terms of human as well as financial resources. The Medicines Agency does not receive any funding from the government and its only source of revenue is registration fees, which have remained unchanged over the past seven years (initially approved in 2003, revised in 2005). Quality control activities do not generate enough income to cover the associated costs. A 0.2% fee on the contract value of awarded tenders and modest revenues from advertisement authorizations are directed to fund activities at the Medicines Agency, although these are inadequate to compensate for the Agency's work. The lack of funding goes some way towards explaining the Agency's inability to fund local (let alone international) inspection activities and the negative impact this lack of resources has on staff retention due to low salaries and motivation.

As an indication, the 2011 WHO PS assessment mission noted that over the past 5 years only 3 of the top 20 producers in terms of the number of registered products were inspected (unpublished report). Inspection and quality assurance is, therefore, an important issue in the light of the high and growing import rates covering approximately one third of publicly procured products from countries which are not automatically considered as compliant with good manufacturing practice (GMP) (e.g. India and China) and, therefore, need to be visited for a GMP inspection before the product can be registered in the Republic of Moldova.³

The ability of the Medicines Agency to carry out inspections and to act quickly is weakened by the limited availability of GMP inspectors (one full-time and one-part time inspector) and by the need to have Ministry approval to inspect manufacturers. Further, there is no enforcement strategy defining applicable sanctions for non-compliance with rules.

3 Either directly or indirectly through organizations with marketing authorizations in Germany and the United Kingdom but with actual manufacturing in Asia.

Licensing of medicines and of facilities

There is no legal requirement for local manufacturers to comply with GMP although various draft regulations exist. As a consequence, of the 25 licensed manufacturers of pharmaceuticals in the Republic of Moldova, only 2 (which export to GMP-compliant countries) are GMP-certified.

There seem to be an overlapping role and ill-defined responsibilities as between the Licensing Chamber and the Accreditation Office in inspecting pharmacies, wholesalers and manufacturers.

There is no legal provision defining inspectors' power and authority, which limits their availability to perform their duties. In addition, funding for inspections is not reliable.

The Medicines Agency is not involved in issuing licences for pharmacies, which means that new pharmacies open without prior inspection.

National good pharmacy practice guidelines have been developed and sent for approval to the Ministry of Health. They are currently under revision.

Quality issues

There are concerns among medical staff in government institutions about the quality and, as a result, about the efficacy of the available medicines. During a WHO mission in 2011, doctors reported problems of sub-standard medicines from China (ceftazidimum) and in locally manufactured medicines (methyl prednisolone and betamethasone). Further, three different medicines with the same batch number were identified in the pharmacy of one of the main hospitals in the capital. These three medicines were sourced from a local manufacturer (non-GMP- and non-GDP-compliant) who was among the tender winners.

One of the key issues affecting the quality of medicines in the country is the focus on quality control rather than quality assurance. The current system is considered unsustainable because it requires a very high number of tests which the national laboratory does not have the necessary capacity to run and, more importantly, it does not seem to be an effective tool for quality assurance. Further, the intensive testing approach very often causes additional delays in the supply chain.

Monitoring and follow-up of blacklisted entities is haphazard. When a blacklist was in place, one of the companies on it bid again under another official entity and there was no legal basis for the Medicines Agency to reject this company in the tendering process.

A recall system for faulty products is available but does not work, as there are no standard operating procedures and no clear legislation assigning this responsibility to the Medicines Agency.

Finally (as indicated in an unpublished WHO report of medicines regulatory assessment in 2011), the cost and regulatory issues involved makes pharmacists reluctant to handle narcotics, which is causing problems with the availability of narcotic painkillers, particularly in rural areas.

Advertising and promotion

There are legal provisions for the control and promotion of pharmaceutical products, and the advertisement of prescription-only medicines and unregistered medicines is forbidden. Enforcement of the rules covering advertising is not, however, fully observed, a situation which is aggravated by the lack of definitions of promotion and advertising and requirements for advertisements.

There is no national code of conduct concerning the advertising and promotion of medicines by holders of marketing authorizations. In particular, the number of samples allowed, online advertisements, gifts to physicians, pharmacists and patients, training, trips and conferences sponsored by the industry are not regulated.

Procurement

Public procurement is conducted by the Medicines Agency at national level. Following the national tendering process, local health care providers sign contracts with the tender winners in order to receive medicines. During visits to both state-owned and private wholesalers by the WHO PS assessment mission in 2011, full compliance with good distribution practice and the use of written formal standard operating procedures was not observed. In addition, owing to limited capacity and (possibly)

limited technical knowledge, the legal requirements for importation, distribution and the methods used for control are inadequate. This could seriously challenge the quality of medicines during transportation and storage.

Import and export

The price is taken into account in the evaluation of the application for importation and if it is perceived as being too high, permission to import is denied. This most likely affects the latest expensive therapies, including orphan drugs.

Pharmacovigilance

There are legal provisions requiring post-marketing surveillance, and a pharmacovigilance system is in place in the Medicines Agency. Some pharmacovigilance functions are performed, although not systematically, and there is no national pharmacovigilance centre linked to the Agency. The lack of reporting of adverse drug reactions is a serious problem. Doctors generally do not report adverse drug reactions due to the fear to be punished for reasons not related to reporting, for example, because they prescribed drugs that are not on the essential medicines list). It is generally part of the physicians' culture to try to avoid every possible contact with regulators.

Price monitoring

The government does not run an active national medicines price monitoring system for retail prices but the Medicines Agency monitors price indicators. Only the prices of the top-selling medicines are monitored rather than the prices of the most essential medicines. This is due to the absence of a system of official monitoring: distributors pay for monitoring and they are interested in collecting useful information for marketing purposes rather than generating new evidence for the benefits of public health policy. Further, there are no regulations requiring retail price information to be publicly accessible.

Pricing and reimbursement of prescription drugs

Pricing of prescription medicines

Outpatient drugs

The prices of outpatient originator medicines are established through external reference pricing based on a basket of 10 countries.⁴ The average ex-factory price of the three lowest prices in the reference countries is estimated and proposed to the manufacturer. There is, however, little negotiation between the Medicines Agency and the manufacturer. On several occasions, manufacturers have refused the price proposed by the Medicines Agency and threatened not to market their products in the Republic of Moldova if the price proposed by the Agency was approved. This has caused delays which, in some cases, have led the Minister of Health to accept the prices proposed by the manufacturer(s).

The lack of flexibility in implementing the external reference pricing methodology has led in some cases to higher prices because one of the three lowest priced countries has a (much) higher price than the other two, thus pushing the average up.

For products which are not registered in other European Union (EU) countries, internal reference pricing is used to set the price. Prices are compared with comparable products (same level four or five of the anatomic therapeutic chemical (ATC) classification system) in the country.

Profits for local manufacturer prices should not exceed 15%. The MoH approves local manufacturer prices according to described internal reference price system and retail margins are capped to 15% of the ex-factory price.

The prices of registered medicines are reviewed annually. The prices of all (first, second, etc.) generic medicines are capped at 75% of the originator brands' prices.

Public and private pharmacies negotiate acquisition prices with distributors, although often distributors own pharmacies. This can lead to variations in the prices of prescription medicines across the country which, given that the national health insurance company reimburses up to a fixed amount for each drug reimbursed,

⁴ Belarus, Bulgaria, Croatia, Czech Republic, Greece, Hungary, Lithuania, Romania, Serbia and Slovakia. On 1 April 2012, the criteria for choosing reference countries were changed to European countries with a population of up to 25 million people. For practical reasons, the list of eligible countries was further reduced to those that were already included in the previous reference list and for which knowledge and experience was already available in extracting prices from the countries' websites or in obtaining them from authorities.

may need to be matched by out-of-pocket payments. Pharmacists, distributors and manufacturers are able to negotiate discounts in transactions between them but the government does not have a clawback system allowing it to retain part of these discounts. Unofficial sources suggest that discounts up to 99% of the cost of some of the most sold medicines exist in the system.

Inpatient drugs

Tendering is used to procure inpatient medicines and medicines for national programmes, such as diabetes (insulin), analgesics (for palliative care), and drugs to treat HIV/AIDS, tuberculosis (TB) and other conditions. Tenders are issued by international non-proprietary name (INN) and both manufacturers and distributors are invited to participate. Contracts are awarded to the lowest price bidder and external reference prices are used as a guide in evaluating the prices offered. Prices are expected not to exceed international reference prices but are not expected to be much lower than these either. The discounts obtained are usually comparatively higher for generics than for originator brands which, for in-patent products, is explained by their monopoly position. The availability of originator brands for patent-expired products is, however, limited.

One of the main problems in obtaining low tender prices is the limited experience in the country in negotiating prices (staff in the Medicines Agency tend to believe that prices proposed by manufacturers are the final prices) and relatively weak bargaining position owing to the small market size.

The 2011 WHO PS assessment mission noted that the national health insurance company reimburses the entire inpatient drug component (€13 million), which represents 10.3% of total expenditure on drugs. In addition the national health insurance company contributes €7 million towards outpatient drugs.

Distribution

The number of pharmacists increased from 5.3 per 10 000 population in 2002 to 7.9 in 2006 and 8.0 in 2009 (16). In June 2011, there were over 978 community-based pharmacies and subsidiaries, of which 350 were network pharmacies and the rest - individual pharmacies. This corresponds to more than 2.4 pharmacies per 10 000

population, representing a decrease since 2005 when there were 3.3 pharmacies per 10 000 population (1111 in the whole country) (6). Pharmacies are not evenly distributed across the country: there are fewer than 1.6 pharmacies per 10 000 inhabitants in the rural regions of Causeni, Cimislia and Nisporeni and more than 4.5 pharmacies per 10 000 inhabitants in the urban areas of Balti, Basarabasca and Chisinau (6).

Distributors' margins are regulated up to a maximum of 15% of the ex-factory price for wholesale mark-ups and up to 25% of the wholesale procurement price for retail mark-ups. There is no regressive or tiered margin structure, which means that these margins are flat.

A value-added tax of 8% is levied on all prescription-only drugs.

Reimbursement

The Ministry of Health decides which medicines will be reimbursed. According to the regulations, reimbursement decisions should be made according to the following criteria: therapeutic efficacy/efficiency, economic efficiency, cost-efficiency, evaluation of the social perspective and price evaluation. In practice, there is no capacity or expertise to evaluate the cost-effectiveness of products and reimbursement decisions mainly rely on the burden of disease in the country as estimated through prevalence and incidence.

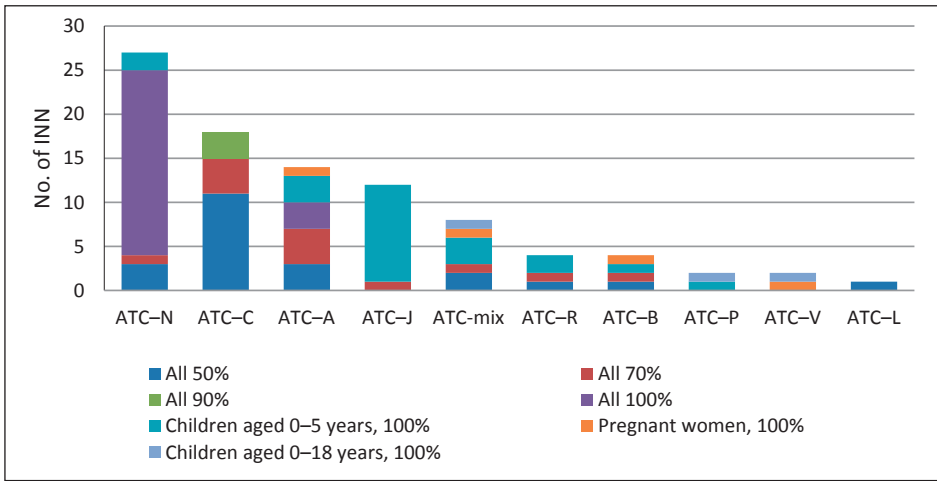
The level of reimbursement is established through data collection from 50 pharmacies across the country. Prices of all available formulations – originator brands, branded and unbranded generics – are collected. The median price of one unit (tablet, capsule or vial) is used to establish the reimbursement price (which is often only a percentage of it).

All drugs dispensed in hospitals are reimbursed but only a small percentage of drugs prescribed in outpatient settings are reimbursed. For outpatient medicines, there is a four-tier reimbursement structure with reimbursement levels at 50%, 70%, 90% or 100%, depending on the price of the drug. The 2011 PS assessment mission noted that the national health insurance company covers on average 50% of outpatient pharmaceutical expenditure on the essential medicines list, totalling €7 million per year in comparison to €13 million of inpatient pharmaceutical expenditure (unpublished observations).

Of the 393 INNs included in the essential medicines list (which was last updated in February 2011), 92 INNs are partially or fully reimbursed for different population subgroups (all, children aged 0–5 years, children aged 0–18 years, pregnant women). Additional drugs such as insulin, analgesics for palliative care and drugs to treat HIV/AIDS, TB and other conditions are available to all free of charge through national programmes.

As shown in Fig. 2, the largest group of reimbursed medicines is neurological drugs (27 INNs in total). Most of these drugs are available to all free (21 INNs), while a smaller number are available either at a reduced reimbursement rate (3 at 50% and 1 at 70%) or only for children aged 0–5 years (2 INNs). The second largest class of reimbursable drugs is cardiovascular drugs (18 INNs), although most of them (11 INNs) are only reimbursed at 50%, followed by alimentary tract and metabolism drugs such as nutrient supplements and diabetes medicines (14 INNs), and anti-infectives, including antibiotic drugs (12 INNs).

Fig. 2. Number of INNs reimbursed by ATC group, reimbursement level and beneficiaries, 2011



Note. ATC-A: alimentary tract and metabolism; ATC-B: blood and blood forming organs; ATC-C: cardiovascular system; ATC-J: anti-infectives for systemic use; ATC-L: antineoplastic and immuno-modulating agents; ATC-N: nervous system; ATC-P: antiparasitic products, insecticides and repellents; ATC-R: respiratory system; ATC-S: sensory organs; ATC-V: various; ATC-mix: different ATC.

Source: Authors' compilation based on the positive list and ATC/DDD Index 2012 (17).

Because the positive list only contains 92 INNs out of a total of 393 INNs in the essential medicines list, and these 92 are often only partially reimbursed and not always for all patients, the list of reimbursable drugs is not enough to meet the basic health needs of the population. This potentially puts disadvantaged socioeconomic groups at serious risk of incurring high and potentially catastrophic out-of-pocket expenditure if they fall ill and need to buy their medicines themselves. This has even greater consequences for chronic diseases, as many drugs are reimbursed at 50% (11 INNs) and only 4 INNs at 70% and 3 INNs at 90%.

Prescribing and generic substitution

Doctors prescribe medicines using brand names. In 2012, as part of the process of revising the order on prescribing and dispensing medicines, the Medicines Agency officially proposed to introduce INN prescribing. However, after extensive discussions within the Ministry of Health and consultations with health professionals and the national health insurance company, the Ministry decided not to introduce INN prescribing.

Another issue arises from doctors owning pharmacies in the clinics or hospitals where they practise (12). Combining clinical practice with drug dispensing can lead to conflicts of interest: doctors have an incentive to prescribe expensive drugs as well as potentially over-prescribe so as to increase their profits from dispensing (18), so supplier-induced demand could be significant.

Generic substitution for prescription medicines is not allowed either for reimbursed or non-reimbursed medicines. For prescription medicines, if the doctor has prescribed a branded medicine the only way to obtain a generic equivalent is to get another prescription from the doctor using the drug's INN. Given the limited availability of originator products in the country (less than 5% of total market share), this does not seem to be a major issue. It may, however, limit savings for the national health insurance company when a more expensive branded generic medicine is dispensed instead of a less expensive non-branded generic one. Considering that the market share of branded generics is 30–35% versus 60–65% for non-branded generics, this is likely to have some impact in terms of potential savings foregone.⁵

⁵ The trade-off in the circumstances facing the Republic of Moldova is savings from cheaper (unbranded) generics versus concerns about the quality of the same medicines.

Procurement and supply

There are three main ways in which pharmaceuticals can be procured or made available in the Republic of Moldova: centralized tendering, hospital tendering and direct purchase by pharmacies. The 2011 WHO PS assessment mission (unpublished report) noted that the pharmaceutical market relies heavily on imported medicines (91.4% of total value) and, to a lesser extent, on local production (8.6% of total value).

In 2006, hospital procurement of medicines and devices was centralized and responsibilities were transferred to the Medicines Agency, which conducts annual tenders. This procurement method is also used for national programmes for the treatment of malaria, HIV/AIDS, TB, sexually transmitted diseases, noncommunicable diseases and the expanded programme on vaccines and immunization. It is not uncommon to have a very limited number of bidders or no bidder at all. If there is only one bidder, the tender is repeated a second time, after which a winner is nominated. In a few instances when only one bidder was available in both rounds, the price in the second tendering round was higher because the bidder knew to be in a monopoly position and the Medicines Agency had to accept the second price offer.

Table 2 presents data on the number of tenders, the budget available, the number of participants, and medicines tendered since the centralized tendering system was established in 2006.

Table 2. Centralized procurement of medicines, including national programmes, 2011

| Procurement | 2006/2007 | 2007/2008 | 2008/2009 | 2009/2010 | 2010/2011 |
|----------------------------------|-----------|-----------|-----------|-----------|-----------|
| Organized tenders | 46 | 41 | 46 | 37 | 57 |
| Budget (million lei) | 316.4 | 328.4 | 391.9 | 375.6 | No data |
| Participants (bidders) (average) | 18 | 17 | 18 | 17 | 20 |
| Medicines | 1288 | 1216 | 1331 | 1551 | 1485 |

Source: WHO Regional Office for Europe (13).

The list of medicines to be tendered for is prepared by the Ministry of Health with the support of the main specialists and is based on the list of essential medicines. This list (using INN) is sent to all hospitals, which in turn provide information on the quantity

needed on an annual basis. Hospitals may procure medicines themselves if these medicines are not included in the tendering list, as long as they are able to provide a valid reason to the Medicines Agency.

In cases of stock-out, hospitals are allowed to extend their existing contracts by up to 30% of the original contracted volume. If this is not sufficient to cover the hospital's needs, a new tender is announced.

Open national tenders are conducted annually with registered manufacturers and distributors. In practice, bidders are mainly distributors and a few local manufacturers. Tenders are awarded to the bidder offering the lowest price. Each hospital receives supplies from the company awarded the tender (there is no central medical store).

Public and private pharmacies, on the other hand, acquire medicines through direct negotiation with wholesalers and/or local manufacturers.

Delays are often caused by the need for the Public Procurement Agency to approve each step in the procurement process and to sign all the contracts, and by legal issues which may arise during the tendering process. In 2010, for example, a dispute over six products which went to court delayed the entire order for all the other 1300 products.

In order to bid, tender participants must have a licence to practise pharmacy and a national GMP certificate (which is generally easy to obtain and does not ensure compliance with GMP), their medicines must be registered and have a remaining shelf life at delivery of not less than 60% for products with an expiry date of over two years and of not less than 80% for products with an expiry date of under two years, including TB medicines. TB medicines and anti-diabetic products should follow GMP (according to the criteria of the WHO, the European Medicines Agency or the Food and Drugs Administration). If there is no GMP-compliant bidder, non-GMP-compliant bidders are accepted.

There is very close involvement of the anti-corruption and competition authority at all stages in the tendering process. Their involvement in the activities of the Medicines Agency can be so close that it sometimes interferes with the Agency's work, even in situations where there is no issue of corruption and competition. This is perceived as limiting the flexibility of the PS chain management system for public procurement. Further, the fact that the mandate of this authority is not well-defined means that it can start investigations without official permission. This has a demotivating impact on the staff involved in public procurement and is probably also partly responsible for the high staff turn-over rate.

Another problem is the conflict of interest between the regulatory function and the procurement function of the Medicines Agency. This leads to pressure to register products quickly, especially if they are less expensive than currently available alternatives, so that they can be included in the next tender. This obviously conflicts with the Agency's responsibility for registration and quality control. Quality is further jeopardised by the lack of pre- and post-qualification of suppliers.

A World Bank report in 2010 (15) made several suggestions to strengthen the public procurement system, including: (i) aligning it with internationally accepted procedures for contract approval; (ii) making the complaint procedure independent of the Medicines Agency to avoid conflict of interest; (iii) addressing work overload issues in the Medicines Agency, which approves more than 100 contracts a day with very limited capacity to carry out these functions; and (iv) developing the required secondary legislation referred to in the public procurement law but which is not yet ready. Finally, the roles and responsibilities of the Medicines Agency need to be revised (15).

Many of the shortcomings in procurement stem from the fact that there are no written implementation procedures apart from public bidding. In addition to open tendering, the law allows for other procurement options such as limited tendering, framework agreement, negotiation, single-source procurement, invitation to quote and e-tenders.

However apart from limited tender and single source procurement, there is a lack of knowledge and experience among the people in charge of procurement and no regulatory implementation procedures exist for these other procurement methods (apart for limited tendering and single-source procurement). In such a scenario, written operational guidelines would help at least in part to address this capacity issue.

Work is continuing in the Public Acquisition Agency to develop e-tender regulations.

All pharmaceutical products imported into the Republic of Moldova have to be batch-tested. GMP-identified manufacturers, in most cases concerning products from Europe, are exempt from testing. For these products a document check is sufficient, which takes two working days to produce. All other products have to be tested (no standard operating procedures provided for this). Owing to the immense constraints on capacity, delays of up to 20 working days are routine, and delays in testing are one of the most common reasons for drug shortages. In general, the supply of essential drugs to date is quite reliable and stock-outs of basic products are the exception rather than the norm.

Inequity in access to medicines

Pharmaceutical coverage as part of national health insurance is limited, causing high levels of out-of-pocket expenditure for patients (12,19). The situation is exacerbated by a weak safety net for lower socioeconomic groups, which are not exempt from out-of-pocket payments, and it is even worse for elderly people who need to pay for the full cost of medicines not included in the limited drug benefit basket. It is slightly better for noncommunicable diseases (such as diabetes) and some infectious diseases (such as HIV/AIDS and TB), as access to some of the medicines needed to treat these diseases is provided free of charge through national programmes funded by donors such as the Global Fund.

All medicines reimbursed in inpatient settings are fully reimbursed by the national health insurance company for insured people, potentially leading to patients accessing tertiary care to obtain free medicines. In 2011, the PS assessment mission noted that the national health insurance company paid €13 million for inpatient medicines out of a total €100 million paid for hospital services (unpublished observations). For reimbursed medicines dispensed in an outpatient setting (either public family doctor centres or private pharmacies), the national health insurance company pays a fixed amount and the patient contributes the remainder, which is usually about 50% of the total drug price.

Analysis of problems in access to medicines

Much of the information in this section of the report is from a medicine price and availability survey conducted in 2011. The survey collected data on 50 medicines (all on the essential medicines list) in 50 public sector pharmacies (outpatients) and 50 private pharmacies in the northern, central and southern regions of the country. Data were collected on originator brands (17 were registered out of the 50 sample medicines), the most sold generics (50), and the lowest-priced generics (50) in each facility, leading to a total sample of 117 drugs. The survey did not include the territories on the left side of the river Nistru and the town of Bender (Transnistria).

Availability

The indicator used represents the overall mean availability of each of the samples of medicine in the facilities surveyed.

Mean availability on the day of data collection was poor at 51.2% in public sector pharmacies (outpatients) and 58% in private retail pharmacies (Table 3). Of these medicines, the availability of originator brands was 15% and 23% in the public and private sectors, respectively; the availability most sold generics were 40% and 46%, respectively, and the availability of lowest- priced generics were 49% and 56%, respectively (Table 3).

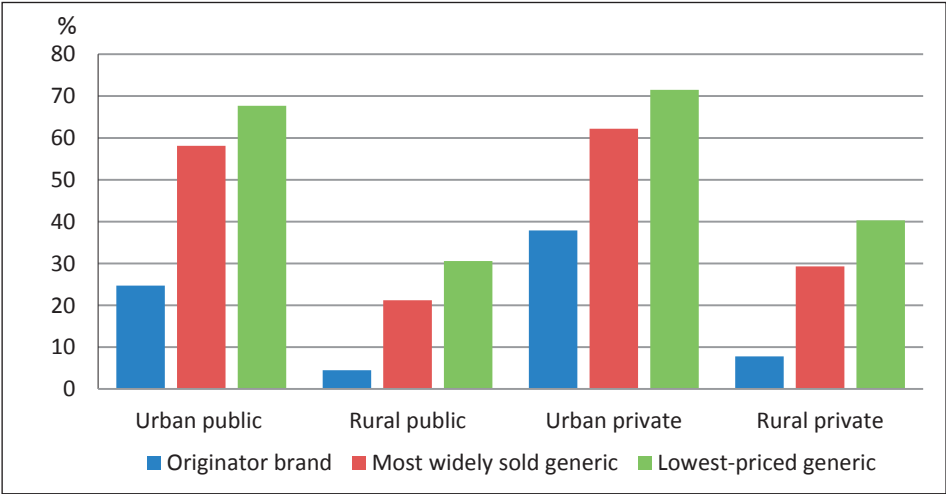
Table 3. Mean availability of medicines in the public and private sector, 2011

| Product type | Mean availability (%) | |
|--------------------------------|-----------------------|----------------|
| | Public sector | Private sector |
| Originator brands (n=17) | 15 | 23 |
| Most sold generics (n=50) | 40 | 46 |
| Lowest- priced generics (n=50) | 49 | 56 |
| Any product type | 51 | 58 |

Source: WHO Regional Office for Europe (13).

Availability in urban areas was higher in both public and private pharmacies for all product types. Originator brand medicines were available in 25% of urban and 5% of rural public pharmacies, and in 38% of urban and 8% of rural private pharmacies. The availability of the most sold generics was better but still low, at 58% of urban and 21% of rural public pharmacies, and in 62% of urban and 29% of rural private pharmacies. Overall, availability was highest for the lowest- priced generics, which were available in 68% of urban and 31% of rural public pharmacies, and in 72% of urban and 41% of rural private pharmacies (Fig. 3).

Fig. 3. Pharmacies where medicines from the list were available, 2011



Data on the availability of individual medicines shows that five originator medicines are not available in public pharmacies and four are not available in private pharmacies. Only three of the generics were not available in any of the public pharmacies surveyed (clonazepam, clozapine, phenoxymethylpenicillin) and three were not available in any of the private sector pharmacies surveyed (clonazepam, clozapine, isosorbide dinitrate). None of the originator brands was available in more than 81% of both public and private pharmacies, while 10 generics were available in 81–99% of public pharmacies and 13 in private pharmacies, with 1 medicine (generic omeprazole) available in all the private pharmacies surveyed (13).

Availability of all product types was higher in chain pharmacies in the private sector compared with individual pharmacies (Table 4). There was not a single pharmacy, whether public or private, where all 50 medicines surveyed were available on the day of the survey.

Table 4. Availability of medicines in chain and individual pharmacies, 2011

| Medicine | Chain pharmacies (%) | Individual pharmacies (%) |
|-------------------------|----------------------|---------------------------|
| Originator brand | 40 | 18 |
| Most sold generic | 65 | 40 |
| Lowest - priced generic | 76 | 50 |

Source: Adapted from (13).

Overall, it appears that location rather than ownership is the determinant of availability, which is explained by the fact that most pharmacist-owned pharmacies are located in rural areas which are characterized by lower levels of availability in comparison to urban areas, as shown by the survey results.

In summary, the availability of medicines was higher in urban than in rural areas and was higher for lowest-cost generics than for the most sold generics. The availability of originator products was particularly low, but this is not negative given that all the medicines surveyed are out of patent and generic alternatives exist on the market. The issue is the poor availability of these generic alternatives.

Prices

Two types of price comparison were made as part of the medicines access survey in order to help understand price levels in the country and their variation by type of medicine, geographical location and dispensing outlets.

The first compared prices in the Republic of Moldova against international reference prices from the *International drug price indicator guide 2010 (20)*. These reference prices are the medians of recent procurement prices offered by for-profit and not-for-profit suppliers of generic products. These suppliers typically sell in bulk to governments or large nongovernmental organizations, and their procurement prices are therefore relatively low and represent efficient bulk procurement without the costs of shipping or insurance. The 2010 international reference prices were available for all the sample medicines. Prices are expressed as a median price ratio (MPR), that is, the unit price in the Republic of Moldova divided by the 2010 international reference unit price converted to local currency using the exchange rate on the first day of data collection. When the MPR equals one, the local price equals the reference price; when the MPR equals two, the local price is twice as high as the reference price.

The second compared prices in the Republic of Moldova against prices in six other European countries (Bulgaria, Germany, Hungary, Italy, Lithuania and Romania).

Comparison of prices in the Republic of Moldova with international reference prices

MPRs in the public and private outpatient sectors

Table 5 shows that MPRs in the Republic of Moldova are much higher than international reference prices. The biggest difference was observed for originator brands in the private sector (8.77 times higher in the Republic of Moldova compared to the international reference prices). Overall, variations between minimum and maximum prices tended to increase with rising prices of medicines.

Although these MPRs show that median patient prices in the Republic of Moldova are four to nine times higher than international reference prices, the magnitude of this difference is inflated because the 2010 MSH international reference prices are procurement prices based on bulk tendering prices and do not include distribution mark-ups and taxes (while patient prices in public and private facilities do). Even when these add-on costs are taken into account, however, it appears that median patient prices in the country are higher than international reference prices.

A comparison of medicines found in both sectors showed that overall originator medicines were priced 6.3% higher in the private sector compared to the public sector (13). While the most sold generics were priced similarly in both sectors, the lowest-priced generics were priced 10.8% lower in the private sector than in the public sector (13).

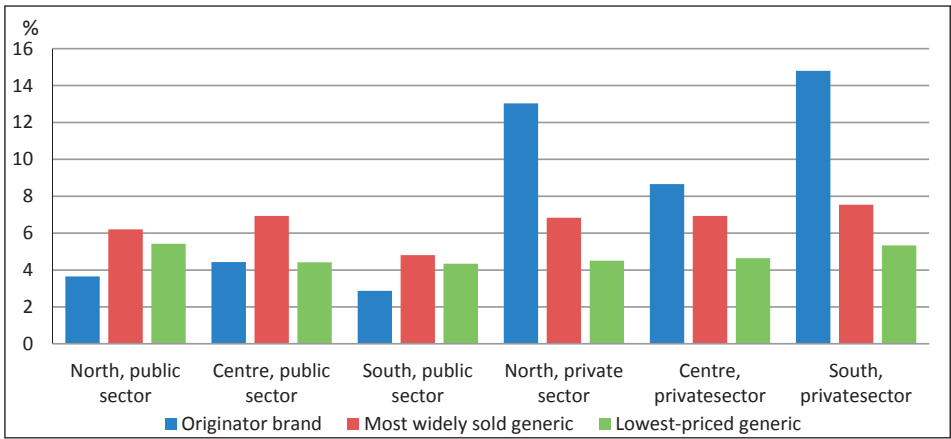
Table 5. MPRs for pharmaceuticals in the public and private sectors, 2011

| MPR | Originator brand | | Most sold generic | | Lowest- priced generic | |
|---------------------|------------------|----------------|-------------------|----------------|------------------------|----------------|
| | Public sector | Private sector | Public sector | Private sector | Public sector | Private sector |
| Median MPR | 7.64 | 8.77 | 6.72 | 6.78 | 5.22 | 4.65 |
| 25th percentile MPR | 2.76 | 3.44 | 3.23 | 3.30 | 2.90 | 3.03 |
| 75th percentile MPR | 18.74 | 29.02 | 9.36 | 9.76 | 7.28 | 7.12 |
| Minimum MPR | 0.45 | 0.46 | 0.64 | 0.67 | 0.64 | 0.64 |
| Maximum MPR | 117.26 | 125.58 | 82.33 | 84.00 | 43.07 | 44.30 |
| No. of medicines | 8 | 10 | 42 | 42 | 45 | 43 |

Source: WHO Regional Office for Europe (13).

An analysis of price differences between the geographical regions showed that originator brands in the public sector were priced highest in the central region compared to the north and south, although few prices were found (Fig. 4). The most sold generics were also priced the highest in the central region. The lowest- priced generics were priced the highest in the north but were similar in price in the centre and south. Conversely, in the private sector, the median prices of originator brands were lowest in the central region, although the analysis was based on only a few medicines. The prices of the most sold and the lowest- priced generics in the private sector were similar across the three regions (Fig. 4).

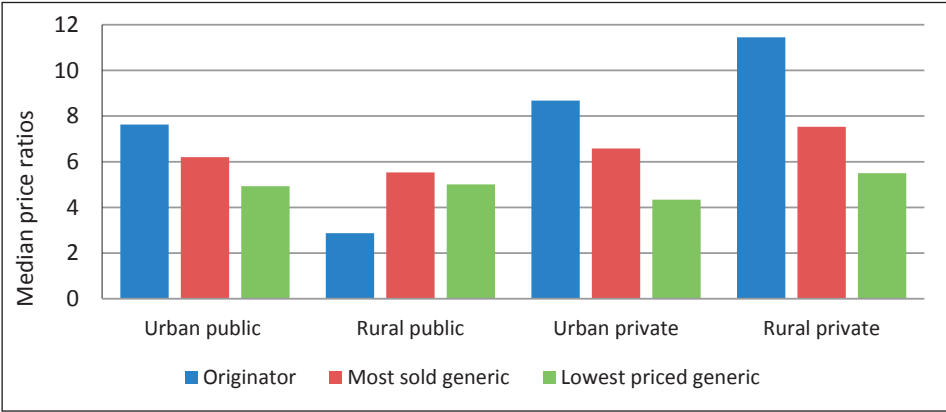
Fig. 4. MPRs for pharmaceuticals by geographical region, public and private sectors, 2011



Source: WHO Regional Office for Europe (13).

In the public sector, overall prices to patients for originator brands were much higher in urban than rural areas, although there were only a few medicines in the dataset. For generics, there was little price variation between urban and rural areas (Fig. 5). In the private sector, prices in rural areas were higher than in urban areas for all three product types.

Fig. 5. MPRs for pharmaceuticals by urban and rural areas, public and private sectors, 2011



Source: WHO Global health expenditure database (4).

MPRs for centrally tendered inpatient medicines

Table 6 shows that median prices in the country are 1.68 to 2.39 times higher than international reference prices. In comparison to MPRs in the outpatient sector, these data show a more contained median price difference, which further supports the argument of the inflated ratios when comparing international reference prices from bulk tendering with prices paid by patients at pharmacies in the country. In this case, the results in Table 6 are based on a fair comparison, “like with like”, as only bulk tendering data were used to calculate the ratio.

Table 6. MPRs for centrally tendered medicines, 2011

| MPRs | Originator brands | Most sold generics | Lowest- priced generics |
|---------------------|-------------------|--------------------|-------------------------|
| Median MPR | 2.39 | 2.36 | 1.68 |
| 25th percentile MPR | | 0.84 | 1.04 |
| 75th percentile MPR | | 5.31 | 3.67 |
| Minimum MPR | 0.40 | 0.53 | 0.44 |
| Maximum MPR | 4.38 | 31.90 | 31.90 |
| Number of medicines | 2 | 17 | 45 |

Source: WHO Regional Office for Europe (13).

Comparison of prices in the Republic of Moldova with prices in six European countries

This sub-section compares median retail in the Republic of Moldova with median prices in four other eastern European and two central European countries.

Table 7 compares retail prices for originator brands in the private sector, but there are too few products in the comparison to draw reliable conclusions.

Table 7. MPRs for originator pharmaceuticals in the private sector, 2011

| Comparator countries | Median ratio comparator country | Minimum ratio | Maximum ratio | No. of medicines |
|----------------------|---------------------------------|---------------|---------------|------------------|
| Bulgaria | 0.84 | 0.72 | 1.27 | 5 |
| Germany | 0.27 | 0.09 | 0.98 | 6 |
| Hungary | 1.17 | 1.09 | 1.63 | 4 |
| Italy | 0.65 | 0.08 | 2.60 | 5 |
| Lithuania | 1.01 | 0.62 | 1.34 | 8 |
| Romania | 1.13 | 0.87 | 4.88 | 6 |

Source: WHO Regional Office for Europe (13).

Based on prices reported by countries, median prices to patients in the Republic of Moldova for the lowest- priced generics were 11% lower than those in Bulgaria (MPR=0.89), 87% lower than in Germany (MPR=0.13) and 64% lower than in Italy (MPR 0.36); similar to those in Hungary and Lithuania, but 13% higher than in Romania (MPR=1.13) (Table 8).

Table 8. MPRs for the lowest- priced generic pharmaceuticals in the private sector, 2011

| Comparator countries | Median ratio comparator country | Minimum ratio | Maximum ratio | No. of medicines |
|----------------------|---------------------------------|---------------|---------------|------------------|
| Bulgaria | 0.89 | 0.40 | 2.67 | 19 |
| Germany | 0.13 | 0.02 | 0.73 | 20 |
| Hungary | 0.96 | 0.15 | 4.40 | 18 |
| Italy | 0.36 | 0.07 | 1.40 | 15 |
| Lithuania | 0.95 | 0.07 | 2.00 | 20 |
| Romania | 1.13 | 0.5 | 4.00 | 19 |

Source: WHO Regional Office for Europe (13).

These comparisons are, however, affected by two main limitations. The first, for originator products, is the restricted number of drugs upon which the comparison is based (four to eight, depending on the comparator country). Given the wide price variations observed across the sample of 50 drugs (Table 5), it is likely that the small sample of drugs used to calculate the MPR in Table 7 is insufficient to give a representative picture of the overall price differences. Second, comparisons are affected by the number of off-list price discount agreements in place in most of the comparator countries. In Germany discount agreements are widely used (21), as in Hungary, Italy and Lithuania, where a limited number of price-volume agreements are implemented (22–24). In countries where off-list price discounts, price-volume agreements, outcome guarantee agreements or claw-back agreements are in place, reported prices will mislead price comparison and lead to lower MPRs.

In summary, median prices in the Republic of Moldova may not be as low as estimated by the data shown in Table 7 in the case of Germany and Italy, for example. If a number of price-volume agreements for the sample drugs are in place in Lithuania, the median prices in the Republic of Moldova could actually be higher, but this also depends on the representativeness of sample drugs. Indeed, minimum and maximum ratios in the Republic of Moldova in comparison to Lithuania indicate a rather wide variation (0.07–2) in median price differences.

Comparison of ex-factory prices revealed that median prices in the Republic of Moldova are 14% higher than in the other six comparator countries and 44% higher than in Romania (12). These estimates are based on a total of 55 cases.

Comparison of catalogue prices with tender prices for inpatient medicines

The ability of the tendering process to secure lower prices for medicines was investigated by comparing tendering prices for a sample of 234 medicines tendered for in 2011 with their catalogue prices. The results showed that the catalogue prices were higher than the tendered prices (median 7.51%) (Table 9).

Table 9. Median deviation of catalogue prices from tendering prices

| Median price deviation | Deviation (%) |
|------------------------|---------------|
| Minimum deviation | -59.95 |
| Maximum deviation | 686.47 |
| Median deviation | 7.51 |
| 25 percentile | -11.44 |
| 75 percentile | 50.54 |

Source: based on publicly available tendering data.

Price components

Price component data were collected for six medicines (clarithromycin, diclofenac, salbutamol inhaler, fluconazole, loratadine and paracetamol) in urban and rural areas in the public and private sectors (originator brands and generics). Starting at the point of sale in a pharmacy, price data were traced back through wholesalers/distributors and retailers (through invoices and interviews) to determine the components of the final patients price.

Almost no difference was observed in the wholesalers' mark-up between sectors, product types, areas and source of manufacture (14.5–14.97%) (Table 10). Retail mark-ups were, however, higher than wholesalers' mark-ups, except in the public sector in rural areas.

Table 10. Price mark-ups by area, product type, source and sector (based on a sample of six medicines), 2011

| Area | Product type | Source | Wholesale mark-up | | Retail mark-up | | Cumulative mark-up | |
|-------|--------------|----------|-------------------|-------------|----------------|-------------|--------------------|-------------|
| | | | Public (%) | Private (%) | Public (%) | Private (%) | Public (%) | Private (%) |
| Urban | Originator | Imported | 14.97 | 14.97 | 20.16–22.79 | 21.20–24.91 | 47.18–49.39 | 47.65–51.68 |
| | Generic | Imported | 14.50–14.97 | 14.97 | 22.77–24.98 | 20.71–22.95 | 49.36–51.78 | 47.12–49.59 |
| | Generic | Local | 14.97 | 14.97 | 22.61 | 24.43 | 48.59 | 50.55 |
| Rural | Originator | Imported | 14.97 | 14.97 | 14.67–15 | 24.68–24.95 | 40.87–40.92 | 51.47–51.75 |
| | Generic | Imported | 14.97 | 14.87–14.97 | 14.93–14.98 | 18.08–25 | 40.59–41.53 | 44.19–51.78 |
| | Generic | Local | 14.97 | 14.97 | 14.73 | 24.13 | 40.08 | 50.55 |

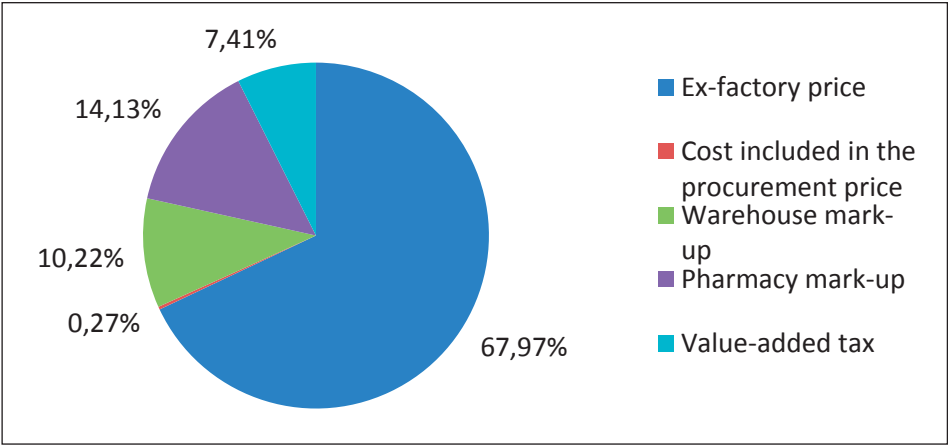
Note. Cumulative mark-ups include 8% value-added tax. Mark-ups do not add up because they were calculated on the landed price or the price calculated after customs clearance and quality control procedures. As a result, they are lower than they would be if they were calculated on the wholesale or retail price.

Source: WHO Regional Office for Europe (13).

Across the six medicines in the price component analysis, the manufacturers' selling price was the greatest contribution to the final price to patients (for originator brands and generics, public and private sector, imported and locally manufactured).

Fig. 6 shows the contribution of each stage to the final price to patients (45.8 lei) for generic imported salbutamol inhaler in the private sector in urban areas. The manufacturers' selling price is 68% of the final price to patients. Very similar data were seen for the originator brands in the private sector and both product types in the public sector.

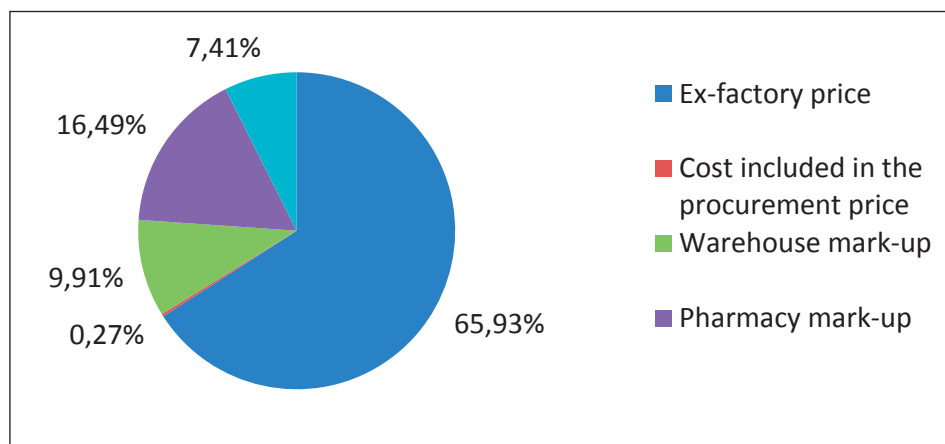
Fig. 6. Retail price components for salbutamol inhaler, generic, urban private sector, 2011



Source: WHO Regional Office for Europe (13).

Fig. 7 shows the data for generic imported salbutamol inhaler in the private sector in rural areas. In this case, the wholesale and retail (pharmacy) mark-ups contribute slightly more to the price to the patient (45.6 lei) but the manufacturers' selling price is the largest contributor at 66%.

Fig. 7. Retail price components for salbutamol inhaler, generic, rural private sector, 2011

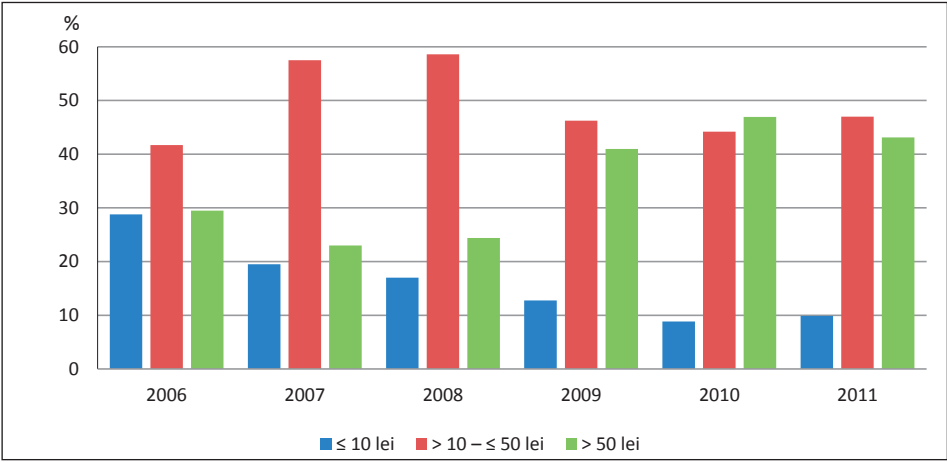


Source: WHO Regional Office for Europe (13).

Price dynamics over time

Fig. 8 shows a decreasing trend in the share of low-priced medicines (≤ 10 lei), as well as an increasing trend in the share of expensive and very expensive medicines. Between 2010 and 2011, however, there was a small increase in the share of low-priced medicines and a small decrease in the share of higher-priced medicines. Overall, the share of medicines priced 10–50 lei has been relatively stable over the last three years, but these figures are based on data from only one wholesaler and are not representative of the entire country.

Fig. 8. Evolution of medicine price groups, 2006–2011



Source: WHO Regional Office for Europe (13).

In summary, the prices of originator products were lower in the public than in the private sector; the prices in the two sectors were similar for the most sold generics, while the prices for the lowest- priced generics were higher in the public sector than in the private sector.

Affordability in the outpatient sector

The affordability of medicine was assessed as the number of days needed by a person on the minimum salary to buy medicines to treat a selection of common acute and chronic diseases, based on standard treatment regimens. At the time of the survey, the daily minimum wage was 20 lei. WHO and Health Action International consider that treatments are unaffordable if a person on the minimum salary has to work more than one day to buy a course of treatment for an acute condition or 30 days’ supply of medicines used to treat chronic diseases.

Table 11 shows examples of some unaffordable treatments in the public and private sectors for medicines to treat both acute and chronic conditions. As shown, those on the minimum wage would have to pay more than half their monthly income to purchase 30 days’ treatment for schizophrenia (clozapine), psychoses (risperidone), Parkinson’s disease (levodopa/carbidopa) and ulcerative colitis (sulfasalazine).

Table 11. Affordability of individual treatments in the public and private sectors, 2011

| Treatment | Days' wages | | | | | |
|---|------------------|-------------------|-----------------------|------------------|-------------------|-----------------------|
| | Public sector | | | Private sector | | |
| | Originator brand | Most sold generic | Lowest-priced generic | Originator brand | Most sold generic | Lowest-priced generic |
| <i>Respiratory tract and other infections</i> | | | | | | |
| Amoxicillin 250 mg capsule x 21 | | 0.9 | 0.9 | | 0.9 | 0.9 |
| Amoxicillin 125 mg/5 ml suspension, 60 ml | | 1.3 | 1.0 | | 1.4 | 1.3 |
| Ciprofloxacin 500 mg capsule x 14 | | 5.1 | 1.5 | | 5.4 | 1.6 |
| Cephalexin 250 mg capsule x 21 | | 1.3 | 1.2 | | 1.3 | 1.2 |
| Clarithromycin 500 mg capsule x 7 | | 6.6 | | 15.5 | 6.8 | |
| Co-trimoxazole 480 mg tab x 14 | | 1.1 | 0.5 | | 1.2 | 0.4 |
| Metronidazole 500 mg tablet x 21 | | | 2.1 | 4.8 | 1.8 | 2.1 |
| <i>Hypertension</i> | | | | | | |
| Atenolol 50 mg tablet x 30 | | 0.9 | 0.9 | | 1.0 | 0.9 |
| Amlodipine 5 mg tablet x 30 | | 3.7 | 3.7 | 3.2 | 3.9 | 3.7 |
| Captopril 25 mg x 30 | | 1.6 | 0.6 | | 1.7 | 0.6 |
| Enalapril 5 mg tablet x 30 | | 2.0 | 1.3 | | 2.4 | 1.8 |
| Enalapril 10 mg tablet x 30 | | 2.3 | 1.7 | | 2.4 | 1.8 |
| Hydrochlorothiazide 25 mg tablets x 30 | | | | | 2.4 | 2.4 |
| Lisinopril 10 mg tablet x 30 | | 3.8 | 2.7 | | 3.9 | 2.9 |
| Verapamil 40 mg x 180 | | 9.3 | 9.3 | | 9.4 | 9.2 |
| <i>Hypercholesterolaemia</i> | | | | | | |
| Simvastatin 20 mg tablet x 30 | | 9.9 | 8.4 | | 10.2 | 6.5 |
| <i>Asthma</i> | | | | | | |
| Salbutamol inhaler 100 mcg x 200 doses | 2.4 | 2.2 | 2.2 | 2.6 | 2.3 | 2.3 |
| <i>Arthritis/analgesia</i> | | | | | | |
| Paracetamol 500 mg tablets x 120 | 3.5 | 1.3 | 1.3 | 3.6 | 1.3 | 1.3 |
| Diclofenac 50 mg tablet x 60 | 17.9 | 1.3 | 1.4 | 19.1 | 1.4 | 1.5 |
| Tramadol 50 mg x 120 | | 8.1 | 8.7 | | 9.2 | 9.3 |
| <i>Ulcer</i> | | | | | | |
| Omeprazole 20 mg x 30 | | 1.7 | 1.7 | | 1.8 | 1.8 |
| Ranitidine 150 mg x 60 | | 2.9 | 2.5 | | 3.0 | 2.2 |
| Famotidine 40 mg x 30 | | 5.0 | 1.8 | | 5.2 | 1.4 |
| <i>Depression/psychoses</i> | | | | | | |
| Amitriptyline 25 mg x 30 | | 2.5 | 2.5 | | 2.7 | 2.6 |
| Imipramine 25 mg tablet x 90 | | 6.5 | 6.5 | | 6.8 | 6.8 |
| Fluoxetine 20 mg tablet x 30 | | 5.0 | 5.0 | | | |
| Clozapine 100 mg tablet x 90 | 46.1 | | | 49.9 | | |
| Risperidone 2 mg tablet x 90 | 31.2 | | | 32.1 | | |
| <i>Other</i> | | | | | | |
| Sulfasalazine 500 mg tablet x 120 | | 15.2 | 15.2 | | 15.8 | 15.8 |
| Levodopa+Cabidopa 250/25 mg x 90 | | 29.3 | 29.3 | | 31.1 | 31.1 |

Table 12 presents the difference in the affordability of medicines for 15 diseases with 40 originator brands (10 originator brands were not found in any pharmacy), the most sold generics, and the lowest- priced generics in the public and private sectors. Given that prices vary across the country, the median average prices of these medicines were used.

Table 12. Affordability of medicines in the public and private sectors, 2011

| Affordability | Number of medicines | |
|---------------------------------------|---------------------------|----------|
| | Price/minimum day wage <1 | % (N=40) |
| More affordable in the public sector | 26 | 65.0 |
| More affordable in the private sector | 8 | 20.0 |
| Identical | 6 | 15.0 |

Source: WHO Regional Office for Europe (13).

The data in Table 12 show that medicines sold in public pharmacies are more affordable in 65% of cases, while those sold in private sector pharmacies are more affordable in 20% of cases. In 15% of cases, the level of affordability is identical for pharmacies in both sectors. Most of the medicines included in the survey were associated with some level of reimbursement: 13 were reimbursed at 50% for all, another 13 at 100% for all, 1 at 90% for all, 8 at 70% for all, 5 at 100% for children aged 0–5 years and 1 at 100% for pregnant women. Only nine medicines were not reimbursed for anyone at any level.

Based on the data on the number of days’ wages needed to buy one month of treatment, there could be affordability problems for lower socioeconomic groups, especially for uninsured people, although given the limited drug benefit basket insured people are also likely to face access issues. This is further supported by evidence of the persistent catastrophic levels of health expenditure faced by both insured and uninsured households (affecting 5.8% of insured and 2.9% of uninsured households in 2010) (9).

Expenditure on essential medicines

The 2011 tendering procurement list (for inpatient medicines only) contained a total of 1032 medicines (dosage- and pharmaceutical form-specific) of which 422 (40.89%) were essential medicines, representing 43.14% of total spending on inpatient medicines (Table 13).

Table 13. Procurement volume for medicines on the lists of essential and non-essential medicines, 2011

| Volume and expenditure | Essential medicines list formulations procured | Non-essential medicines list formulations procured | Total number of formulations procured |
|--------------------------|--|--|---------------------------------------|
| <i>Volume</i> | | | |
| Number of formulations | 422 | 610 | 1032 |
| Percentage | 40.9% | 59.1% | 100% |
| <i>Expenditure</i> | | | |
| Procurement volume (lei) | 113 460 837 | 149 538 306 | 262 999 143 |
| Percentage | 43.1% | 56.9% | 100% |

Source: based on the results of the two largest tenders (Nos.1317/11 of 26 August 2011 and 1817/11 of 14 November 2011).

Rational use of medicines

In theory, physicians should follow prescribing guidelines and prescribe drugs from the essential medicines list. In practice, they prescribe what they prefer without taking rational prescribing principles into account. One of the key issues is the lack of supervision of prescribing. In addition, there is a threat of supplier-induced demand by doctors who own pharmacies. This situation is further exacerbated by weak control of the promotion of medicines to physicians.

Another issue is the practice of pharmacists in charge of dispensing medicines in public pharmacies in primary health care units sometimes to dispense without prescriptions.

A greater effort is needed to promote the rational use of medicines. For example, there is no national programme or committee involving the government, civil society and professional bodies to monitor and promote the rational use of medicines (7). Further, evidence from a recent study of prescribing practices in the country which examined prescriptions in 2011 identified 7.8% cases of overprescribing (26).

Questions about the performance of drug policy

Barriers to availability and affordability of medicines

Current situation. The overall availability of medicines in the Republic of Moldova is limited in both the public and private outpatient sectors (mean availability 51.2% and 58%, respectively). Availability was particularly poor for originator products; it was better, although still limited, for the most sold and the lowest - priced generics. In rural areas it was poorer than in urban areas. This is partly explained by physical barriers to the distribution of medicines and the lack of economic incentive to open pharmacies in rural areas.

Affordability varied between and within drug treatment groups. For respiratory tract and other infections, two drugs out of seven surveyed cost less than one day's minimum wages in the public or private sectors. For hypertension, only two out of eight cost less than one day's minimum wages in the public or private sectors, and one drug cost up to nine working days (verapamil). The highest prices were observed for two drugs for depression, clozapine and risperidone (only available as originator brands), which cost 46.1 and 31.2 days' minimum wages each. Given that not every individual is covered by health insurance, coupled with the limited coverage of medicines as part of the benefit package, high prices pose a severe threat to patients' access to treatment.

Recommendations. It is not clear whether the selection of sample drugs itself was one of the main reasons for low drug availability. These drugs were selected from the Health Action International core list of drugs and essential drugs in the Republic of Moldova. If physicians do not follow rational prescribing principles and prescribe non-essential drugs, which in turn will be procured by pharmacies in preference to essential drugs, the low availability might refer to essential drugs. To assess whether this is true, a survey of the availability of prescribed drugs should be conducted.

Availability in rural areas could be improved by relying on a few large private or public outlets (for instance, part of a chain of pharmacies owned by a distributor) and a local public distribution system to rural health posts. In this way, transport costs for the private

sector would be reduced and economies of scale generated through bulk purchasing by a few large rural outlets, which would then redistribute medicines to local health posts.

In order to assure affordability, health insurance coverage should be extended to the entire population and the scope of the basic benefit package for drugs broadened to include the entire essential medicines list. Special reimbursement conditions (such as exemption from out-of-pocket payments) should apply to the most vulnerable groups such as children, the elderly, chronically ill and disabled people and pregnant women.

Prices of medicines in comparison with other countries

Current situation. According to the official prices published by four eastern and two central European countries, the median prices in the Republic of Moldova for the lowest-priced generics were 11% lower than those in Bulgaria (MPR=0.89), 87% lower than in Germany (MPR=0.13) and 64% lower than in Italy (MPR 0.36); similar to those in Hungary and Lithuania, but 13% higher in Romania (MPR=1.13).

Recommendations. In a number of cases, the list prices in other countries do not represent the actual price paid because of the existence of agreements between payers and manufacturers. The country should consider engaging in some form of discount or price-volume agreements for medicines with a high expected impact on the budget. This would help to bring down the annual expenditure on medicines by granting reimbursement for excess spending. France, for example, has successfully implemented a rebates agreement and Germany likewise a discount agreement.

Another option could be to create regional purchasing groups for a limited number of products (such as small orders) with, for example, Romania, to increase purchasing power. Given that the language requirements for packaging in the Republic of Moldova are Romanian and Russian, this could be feasible.

Prescribing practices with regard to generic and brand medicines

Current situation. Despite a recent attempt to introduce INN in 2012, doctors still prescribe using brand names. Further, generic substitution by pharmacists is not

allowed. If a doctor prescribes a branded medicine, the only way for a person to obtain a generic equivalent is to get another prescription from the doctor using the INN name.

Recommendations. A regressive margin structure should be introduced for wholesalers and pharmacists as an incentive to get them to procure and dispense low-cost generics over high-cost branded medicines. A further incentive for pharmacists to dispense generics could be a reward system in the form of a flat price premium and/or a small percentage reward on the price of each generic prescription dispensed. Examples of countries implementing such systems include Denmark, France and Switzerland.

For generic substitution at pharmacy level to work effectively, information systems should be updated so that even if the branded name is entered into the system, a list of all the available generic options appears.

Medical doctors should be trained to prescribe by INN during their university studies, and labelling requirements should mandate a large-font INN print-out and small-font brand names.

Spending of public funds on essential medicines

Current situation. Only 40.9% of all inpatient medicines procured in 2011 were essential medicines, as against 51.1% non-essential medicines.

Recommendations. The essential medicines list has recently been updated and adapted to the needs of the population in line with WHO recommendations. Since the proportion of essential medicines procured appears to be rather low, efforts should be made to procure more of them so as to improve rational drug use. Such efforts should go hand in hand with promotion of rational prescribing.

Price components and where in the procurement and supply chain the situation could be improved

Current situation. The average wholesale margin in the Republic of Moldova is 14.9%, higher than in most other European countries, ranging from 3% in Sweden to 23% in the Netherlands with the majority varying between 4-8% of the retail price (according to data from 27 countries belonging to the EU since January 2007) (27).

The margin for pharmacies (20.9%) is in line with the European average, which ranges from 12% of the retail price in Romania and 50% of the retail price in Luxembourg (according to data from 15 of the 27 countries belonging to the EU since January 2007) (27).

Recommendations. The wholesaler margin is high in comparison with the average in other EU countries and should be lowered. In addition, a regressive margin system should be introduced to give an incentive for generic substitution as well as bulk discounts from wholesalers. The number of bands in the regressive margins structure should be limited to three or four to simplify implementation, although this will depend on the number of available prescriptions and their value. Retrospective analysis of consumption data is needed. Given the wide availability of generic and the modest availability of innovative products, the distribution of the value of available products is likely to be skewed to the right in the Republic of Moldova. In such situation it might be preferable to have two to three bands where most medicines are concentrated, and a larger band for products with lower frequencies. Above all, the structure of the margins needs to make sense for pharmacists, as they must not be disincentivised to stay in the market.

Assurance by the regulatory system that only good quality medicines are on the market

Current situation. There are issues of resource constraints, in terms of both human and financial resources, when it comes to inspection of new suppliers, particularly suppliers in the far east such as China and India. There is only one GMP inspector in the whole country and regulations do not include fees for inspections. Other issues include the lack of clear regulation, fees and the high number of applications from the Asian region.

Recommendations. It could be helpful for the Republic of Moldova to collaborate with other countries (such as neighbouring countries like Romania) and share responsibilities and costs for overseas inspections.

Since it is impossible for all manufacturers to be covered, registration of medicines should be limited to countries with stringent regulatory authority.⁶

The system needs to move from the current focus on quality control to quality assurance.

⁶ A stringent drug regulatory authority is a regulatory which is (a) a member of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), or (b) an ICH observer, or (c) a regulatory authority associated with an ICH member through a legally binding mutual recognition agreement.

Limitations

This study is subject to several limitations, including a few cases of divergent evidence from different data sources which have been documented in footnotes. Owing to time constraints, it was only possible to have a few exchanges via telephone and e-mail with representatives of the Medicines Agency and the academic world, which limited the ability of the study to make a more in-depth analysis of some of the issues identified.

Comparison of prices in the Republic of Moldova with list prices in other European countries is affected by the presence of discounts off list prices (for example price volume agreements, rebate contracts, etc.) in most European countries.

Conclusions and recommendations

The activities of the Medicines Agency, which combine oversight, regulation and procurement, are creating conflicts of interest.

Regulations are not keeping pace with actual operational requirements. In addition, there is a strong influence, in practice not limited to oversight, by the Public Procurement Agency (the agency is part of the Ministry of Finance) which is causing substantial delays and, in a number of cases, hampering access to the most essential drugs. The lack of adequate operational regulations is leading to a lack of opportunity to use mechanisms other than centralized procurement.

The main issues uncovered during the four studies and recommendations for addressing them are listed below.

Availability

Issues

- The geographical distribution of pharmacists and pharmacies is uneven.
- The availability of medicines in both the public and private sectors is poor.
- Remote areas are particularly affected by the limited availability of medicines owing to infrastructural problems (such as the limited road network) and the lack of economic incentives for pharmacists or distributors' networks to open pharmacies in these areas.

Recommendations

- An incentive system could be introduced to encourage young pharmacists to work in rural areas. Experience with graduate medical doctors has shown that compulsory rural service works. It could be complemented through salaries and/or other benefits such as accommodation allowances. Incentives such as higher retail margins should be offered to pharmacy owners to promote more pharmacies in rural areas.
- The reasons for the limited availability of medicines need to be better understood and addressed. This could be done through interviews with pharmacists and wholesalers to understand where the bottlenecks are.

Prices

Issues

- Comparison of ex-factory outpatient prices in the Republic of Moldova with prices in six European comparator countries shows that the country is affected by high ex-factory prices. A similar issue was identified for tendering prices, which were only slightly lower (median 7.51%) than catalogue prices. This seems to be due to the limited skills and experience in price negotiation, coupled with reduced bargaining power because of the small market.
- Savings from wholesale or retail discounts only benefit the supply chain as there is no clawback system to transfer part of these savings to the national health insurance company.

Recommendations

- Training in price negotiation is needed for staff involved in tendering and purchasing outpatient medicines.
- A clawback system should be introduced to recover part of the savings obtained by wholesalers and retailers, but designed so that distributors do not lose the incentive to negotiate over prices.
- A system to monitor prices should be introduced.

Affordability

Issues

- The majority of drugs remain unaffordable owing to high prices, incomplete coverage and limited benefits for drugs under the social health insurance.
- The list of reimbursed drugs is very limited and there are weak protection mechanisms for the chronically ill and the elderly.

Recommendation

- Universal health coverage and the comprehensiveness of the basic benefit package for drugs should be broadened and safety-nets introduced for vulnerable groups.

Registration

Issues

- Pressure from local and foreign manufacturers to register products quickly and a lack of resources to inspect suppliers are leading to several marketing authorizations being granted without ensuring compliance with GMP.

- The bioequivalence of generic with originator medicines is not being assessed.
- The current system relies on quality control and involves a large number of quality tests. Apart from the limited ability of this system to ensure quality, it is also consuming a very considerable amount of resources.
- The Medicines Agency does not receive any funding from the government and its only revenue comes from modest sources, such as registration fees, which have not been revised in the past seven years, quality control activities which do not even generate enough revenue to cover the costs, a 0.2% fee on the contract value of awarded tenders although this is not adequate to pay for the Agency's work, and a modest revenue from advertising authorizations.
- The number of staff in the Agency and their level of training are not commensurate with the workload and the level of expertise required by their posts.
- Temporary and conditional approval is not clearly defined in the legislation, although it is being implemented by the Ministry of Health.
- Responsibility for registration (Agency Director or Minister of Health) is unclear.
- The new law mandates 210 days to register a medicine, whether branded or generic (European requirements mandate for 210 days to register a branded medicine and 90 days to register a generic medicine).

Recommendations

- There is a need to move from the current system of quality control to a system of quality assurance based on manufacturers' compliance with GMP. Such compliance needs to become a legal requirement.
- In order to contain expenditure on quality assurance while still assuring quality, the registration of medicines should be limited to those registered in countries with stringent regulatory authorities.
- The development of bioequivalence guidelines, which was started in 2012, should be completed and inspectors trained in the assessment of bioequivalence.
- Risk assessment should replace analysis of every registration sample.
- Issues related to the high turnover rate in the Agency should be addressed; stable funding for human resources ensured and staff remunerated according to their duties and the level of expertise required; staff should be provided with clear job descriptions which reflect their realistic duties on a day-to-day basis; and they should be trained and offered opportunities for continuing development.
- Conditions for temporary and conditional approval in regulations should be defined.

- The person responsible for registration (the Agency's Director or the Minister of Health) should be defined in the law. In the interests of saving resources, it would be advisable that this should be the Agency's Director.
- The registration timeline should follow European requirements.

Licensing

Issues

- There is no requirement for manufacturers, wholesalers and distributors to comply with GMP and good distribution practice.
- National good pharmacy practice guidelines are still being revised and are not yet available or being implemented.
- There is no legal requirement for pharmacists to be registered.
- Sometimes doctors own pharmacies, creating a conflict of interest which could lead to overprescribing issues.
- There is an overlap of roles and ill-defined responsibilities between the Medicines Agency, the Licensing Chamber and the Accreditation Office in relation to the inspection of pharmacies, wholesalers and manufacturers.
- Inspectors often lack the required (and continuing) training in areas such as GMP, good clinical practice, good laboratory practice and good distribution practice.
- Inspectors' power and authority are not defined in the legislation.
- The Medicines Agency does not have the necessary resources to inspect with the frequency stated in the law.
- The Medicines Agency needs the Ministry's approval to inspect manufacturers.
- There is no enforcement strategy defining sanctions applicable for non-compliance with rules.

Recommendations

- The draft legislation requiring manufacturers to comply with GMP should be finalized and enforced.
- Legal provisions requiring wholesalers and distributors to comply with good distribution practice are needed.
- GMP, good distribution practice and national good pharmacy practice guidelines need to be published by the government and implemented.
- Legal provisions are needed requiring pharmacists to be registered.
- Regulations are needed to prevent conflicts of interest for doctors who own pharmacies.
- The final goal should be to delegate responsibility for inspection activities entirely to the Medicines Agency. While working towards this, the roles

and responsibilities of the Medicines Agency, the Licensing Chamber and the Accreditation Office need to be defined in order to avoid overlap. Good communication and collaboration between the three agencies is essential.

- Inspectors need to be provided with continuing training so as to carry out their duties in a complex and dynamic regulatory environment. They also need to be provided with the power and authority to carry out their services. The extent of these should be clearly described in the law.
- The Medicines Agency needs a stable income to work efficiently. Possible sources of revenue should be reviewed and the fee structure for its services revised.
- The Ministry of Health should delegate the authority for inspection and enforcement to the Medicines Agency.
- A plan with clear deadlines to achieve compliance with good manufacturing, clinical, laboratory and distribution practices should be developed.

Market control and quality

Issues

- The current system is based on quality control, carrying out a very large amount of sample testing with a dubious impact on quality.
- There is no functional recall system for faulty products.
- The system for handling narcotics is overly restrictive and expensive and affecting the availability of painkillers.
- There is anecdotal evidence about the quality of medicines but the extent of the problem is not known.

Recommendations

- The focus on quality control should change to a system of quality assurance developed by the manufacturer and controlled by the Medicines Agency.
- The number of samples for testing should be based on risk-assessment estimates.
- Standard operating procedures for recalling drugs should be developed, and their efficiency should be tested and evaluated.
- While making every effort to ensure the appropriate use of narcotics and prevention of abuses, regulations need to be relaxed so that pharmacies will be more willing to store narcotic painkillers.
- National quality control laboratories should be encouraged to participate in international schemes such as the WHO external assessment of official quality control laboratories, the WHO prequalification medicines programmes, the

European Centre for Disease Prevention and Control network of biological laboratories, and the Official Medicines Control Laboratories network of the European Directorate for the Quality of Medicines & Health Care.

- A baseline study to assess the extent of the problem with and key issues in assuring the quality of drugs would be useful, with the objective of moving towards a system of quality assurance and compliance with good manufacturing and good distribution practices. This would allow assessment of the impact of the measures implemented, such as the introduction of quality management and mandatory compliance with good manufacturing and good distribution practices.
- Generic substitution should remain the over-arching policy objective, although decision-makers need to be mindful about the quality issues in the supply of generic medicines. Quality concerns may render generic substitution ineffective and need to be addressed vigorously through inspections, a programme of extensive testing, accreditation of the relevant laboratories, capacity-building in these laboratories (where needed), and rationalization of the generic medicines in the supply of drugs.

Advertising and promotion

Issues

- There is a lack of regulatory requirements in a number of areas such as the number of samples allowed, advertising on the internet, and gifts from the industry to physicians, pharmacists and patients.
- Enforcement of the rules for advertising is weak.

Recommendations

- Advertising requirements should be in line with EU regulations.
- Advertisements by doctors and physicians should be prohibited.

Procurement

Issues

- Conflicts of interest could arise in the Medicines Agency because of its responsibilities for both the regulation and procurement of medicines.
- Centralized procurement is subject to delays and lack of flexibility.
- Although tender contracts include penalties for failure or delay in supplying the market, they are rarely applied in cases of failure. The main reasons for hospitals

not to sue manufacturers are the time involved and the urgent need to find an alternative supplier.

- It is not unusual to have only one bidder or no bidder at all for a centralized tender.

Recommendations

- Procurement should be independent of the Medicines Agency so as to avoid conflicts of interest with the Agency's other regulatory functions, such as registration.
- Procurement should be outsourced and centralized procurement limited.
- Central procurement should be limited to around the 300 most commonly needed drugs, while the bulk of procurement should be decentralized to hospitals.
- The procedure for suing manufacturers who break the conditions for supplying drugs set out in tender contracts should be made efficient. A simple and fast procedure would encourage hospitals to act legally against manufacturers who breach contracts and provide a deterrent for such behaviour to happen again.
- Tenders should be published in English as well as the local language and advertised internationally (ideally using EU channels).
- The coordinating and oversight roles of the Public Procurement Agency should not become a reason for delays in tendering times.
- For the country to become an attractive market for manufacturers, it is essential that regulatory capacity is strengthened by gradually bringing it into alignment with EU standards. This will raise the profile of the regulatory agency and will encourage manufacturers to do business in the country. Alignment with EU regulations is a long process, so a priority list and timeline for reforms should be prepared in consultation with WHO and possible business partners (manufacturers who do not yet sell their drugs in the country but who might do so if the necessary reforms are implemented). GMP requirements should be one of the top priorities for the country to become an attractive market.
- In the meantime, and while the necessary reforms begin to be implemented, the following options should be considered to ensure a reliable supply of essential medicines: (i) direct imports, (ii) parallel imports, (iii) requests for assistance only to be addressed by EU countries because this will ensure that quality medicines will be imported, and (iv) (as a last resort) manufacturers to be informed of plans to use compulsory licensing for the procurement of innovative medicines.

Import and export

Issue

- If the price of a medicine is higher than the registration price, authorization to import is denied.

Recommendation

- Price should not play a role in evaluating import applications in order not to detriment availability of innovative medicines.

Distribution

Issue

- There is a very large number of wholesalers in the Republic of Moldova who do not generally specialize in a particular therapeutic area but procure most of the medicines sold in the country, even if this means making frequent and small orders. This creates an additional burden for the Medicines Agency in terms of quality control and duplication of testing for the same medicine from all wholesalers.

Recommendations

- Revising the wholesalers' mark-up can generate the necessary incentive to wholesalers to move toward a more efficient structure and presence in the country.
- The Medicines Agency should hold the licence to sell a particular medicine and should deal directly with the medicines procurement agency. Distributors should only distribute the medicines.

Rational use

Issue

- There is scope for significant improvement in the rational use of medicines.

Recommendation

- A national programme to monitor and promote the rational use of medicines should be established and the involvement of professional bodies and civil society in such activities fostered.

Post-market pharmacovigilance

Issues

- Pharmacovigilance activities are weak and need strengthening.
- There is little reporting by physicians.
- It is unclear whether any analysis of the data collected is conducted.

Recommendations

- A national pharmacovigilance centre linked to the Medicines Agency should be established to ensure coordination of these activities.
- Reporting should be facilitated through the establishment of an online reporting system and barriers to low reporting should be addressed. This could be done by establishing a dialogue with physicians, removing penalties which, although not related to reporting, may apply in cases of reporting (such as sanctions against a physician for dispensing drugs not on the essential medicines list), training physicians in reporting and including all physicians in the obligation to report.
- The Agency needs to analyse the data collected and react to the findings.
- Pharmacovigilance legislation should be updated and made compliant with EU law.

References

1. Statistica Moldovei. Statistical data: population [online database]. Chisinau, National Bureau of Statistics of the Republic of Moldova, 2012 (<http://www.statistica.md/index.php?l=en>, accessed 4 September 2012).
2. World Bank database [online database]. New York, World Bank, 2012 (<http://data.worldbank.org/>, accessed 4 September 2012).
3. *World health statistics 2012*. Geneva, World Health Organization, 2012 (http://www.who.int/gho/publications/world_health_statistics/2012/en/, accessed 4 September 2012).
4. Global health expenditure database [online database]. Geneva, World Health Organization, 2012 (<http://apps.who.int/nha/database/DataExplorerRegime.aspx>, accessed 4 September 2012).
5. *World health statistics 2011: indicator compendium*. Geneva, World Health Organization, 2011 (http://www.who.int/gho/publications/world_health_statistics/WH2011_IndicatorCompendium.pdf, accessed 4 September 2012).
6. Health policy note (draft). Chisinau, Government of the Republic of Moldova, New York, World Bank, 2006.
7. *Republic of Moldova: pharmaceutical country profile*. Chisinau, Ministry of Health and Geneva, World Health Organization, 2011 (<http://apps.who.int/medicinedocs/documents/s19093en/s19093en.pdf>, accessed 6 September 2012).
8. *National health policy*. Chisinau, Ministry of Health Republic of Moldova, 2007 (http://ms.gov.md/_files/1002-PoliticaNationala_rom_rus_finall.pdf, accessed 14 September 2012).
9. Shishkin S, Jowett M. *A review of health financing reforms in the Republic of Moldova*. Copenhagen, WHO Regional Office for Europe, 2012 (Health Financing Policy Paper 2012/1) (<http://www.euro.who.int/en/what-we-do/health-topics/Health-systems/health-systems-financing/publications2/2012/20121-a-review-of-health-financing-reforms-in-the-republic-of-moldova>, accessed 4 September 2012).
10. Usatii A. Plenary Session 4. Achieving universal coverage: a key role of health system. Republic of Moldova case. In: *Moving towards universal health*

- coverage: *Health financing matters: 2012; 24–28 January 2012, Bangkok, Thailand* (http://www.pma-conference.mahidol.ac.th/index.php?option=com_content&view=article&id=322:2012-conference-program&catid=989:2012-program&Itemid=138, accessed 11 September 2012).
11. Richardson E et al. Health insurance coverage and health care access in Moldova. *Health Policy Planning*, 2012, 27(3):204–212.
 12. Atun R et al. Moldova: health system review. In: Richardson E, Ancker S, ed. *Health systems in transition*, 2008, 10(5):1–138.
 13. *Medicines prices, availability and affordability, and price components in the Republic of Moldova*. Copenhagen, WHO Regional Office for Europe (in publication).
 14. Duke T et al. Quality of hospital care for children in Kazakhstan, Republic of Moldova, and Russia: systematic observational assessment. *Lancet*, 2006, 367(9514):919–925.
 15. *Republic of Moldova country procurement assessment report*. New York, World Bank, 2010 (Report No. 61702-MD) (<https://openknowledge.worldbank.org/bitstream/handle/10986/2989/617020ESW0Gray0e0only0900BOX361480B.pdf?sequence=1>, accessed 6 September 2012).
 16. Global atlas of the health workforce [web site]. Geneva, World Health Organization, 2007 (<http://apps.who.int/globalatlas/>, accessed 6 September).
 17. ATC/DDD Index 2012 [online database]. Oslo, WHO Collaborating Centre for Drugs Statistics Methodology, 2011 (http://www.whocc.no/atc_ddd_index/, accessed 8 September 2012).
 18. MacLehose L, in: McKee M, ed. *Health care systems in transition: Republic of Moldova*. Copenhagen, WHO Regional Office for Europe, 2002, 4(5).
 19. Kutzin J, Jakab M. Fiscal context and health expenditure patterns in CEE/CIS countries. In: Kutzin J, Cashin C, Jakab M, ed. *Implementing health financing reform: lessons from countries in transition*. Copenhagen, WHO Regional Office for Europe, 2010:65–82.
 20. Frye J, ed. *International drug price indicator guide*. Cambridge, MA, Management Sciences for Health, 2010 (http://erc.msh.org/dmpguide/pdf/DrugPriceGuide_2010_en.pdf, accessed 6 September 2012).
 21. Stargardt T, Busse R, Dauben H. Germany: pharmaceutical profile. In: Rosian-Schikuta I, Thomson T, ed. *Pharmaceutical pricing and reimbursement information project*. Vienna, ÖBIG/Austrian Health Institute, 2008.
 22. Kovács T et al. Hungary: pharmaceutical profile. In: Thomson T et al., ed.

- Pharmaceutical pricing and reimbursement information*. Vienna, ÖBIG/Austrian Health Institute, 2007.
23. Krukiene G, Alonderis T. Lithuania: pharmaceutical profile. In: Morak S, ed. *Pharmaceutical pricing and reimbursement information*. Vienna, ÖBIG/Austrian Health Institute, 2008.
 24. Martini N, Folino-Gallo P, Montilla S. Italy: pharmaceutical profile. In: Thomson T et al., ed. *Pharmaceutical pricing and reimbursement information*. Vienna, ÖBIG/Austrian Health Institute, 2007.
 25. Safta V et al. Analysis of medicine price evolution in the Republic of Moldova. *Pharmaceutical Magazine of Moldova*, 2008(1–2):3–8.
 26. Safta V. *Naznachenie lekarstv v respublike Moldova [The prescription of medicines in the Republic of Moldova]*. Chisinau, Gosudarstvennii Universitet Medicini i Farmacii imeni Nikole Testemicanu Respubliki Moldova [Nikole Testemicanu Republic of Moldova State Medical and Pharmaceutical University], 2011 (unpublished document).
 27. Kanavos P, Schurer W, Vogler S, The pharmaceutical distribution chain in the European Union : Structure and impact on pharmaceutical prices, EMINET, 2011



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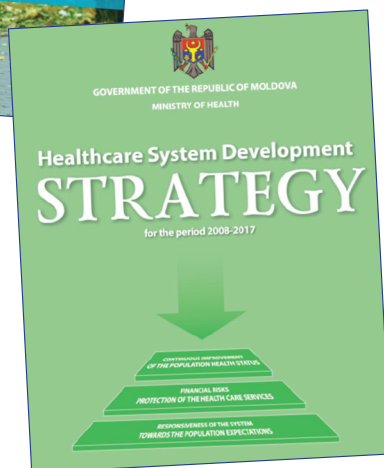
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WHOLIS E96712
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