Republic of Albania

Technical Assistance

Review of Albanian Pharmaceutical Policy

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# Abbreviations

ATC Anatomic Therapeutic Chemical

ARB Angiotensin II Receptor Blockers

BIA Budget impact analysis

CEA Cost-effectiveness analysis

CEE Central and Eastern Europe

CIF Cost, Insurance and Freight

CMA Cost-minimization analysis

CUA Cost-utility analysis

DDD Defined Daily Doses

ERP External Reference Pricing

GDP Gross Domestic Product

GP General Practitioner

HIF Health Insurance Fund

INN International Nonproprietary Name

MoH Ministry of Health

NCDs Non-communicable diseases

NCDC National Center for Drug Control

NICE UK National Institute for Clinical Excellence

OOP Out of Pocket

OTC Over the counter

QSUT QendraSpitaloreUniverstitare “Nene Teresa” – University Hospital Mother Teresa

SMC Scottish Medicines Consortium

QALY Quality adjusted life years

HTA Health Technology Assessment

# Executive summary

The Albanian Ministry of Health is embarking on an ambitious reform of the pharmaceutical sector aiming to rationalize expenditure, improve reimbursement decision making and increase access to medicines. This report provides an overview of the current Albanian pharmaceutical market; analyzes pricing, reimbursement, prescribing and dispensing regulation; and aims to recommend a set of measures to support the efforts of the Ministry of Health. The report is based on available data collected from the MoH, HIF and NCDC and interviews conducted during two missions to Albania in April and June 2014.

**In 2013, Albanian public spending on health amounted to 2.6 percent of GDP, the lowest among countries in the region. Out of pocket expenditures accounted for as much as 55 percent of total expenditures on health (the highest among countries in the region) of which 45% was spent on pharmaceuticals. Nevertheless, the HIF’s expenditure on reimbursed medicines has substantially increased from 2008-2013. Low spending on health care (both in terms of total and public expenditure), high proportion of out of pocket spending and a remarkably low percentage of health insured in the population point to the fact that Albania has historically not considered investing in health care as a priority. It is reasonable to expect that a substantial proportion of ill Albanians are currently not properly** diagnosed and receiving rationally prescribed therapy. Apart from economic hardship, quality of care issues may further influence compliance (and volume of dispensed medicines) in therapy for diagnosed patients. This, combined with the expected rise in the incidence and prevalence of NCDs and other issues may generate substantial potential for escalating expenditure on medicines in the coming years.

**Albania imports most of its drugs, however there are a few domestic manufacturers that produce a number of essential drugs . The number of wholesaler seems fairly high having in mind both the size of the population and the market, when compared to most western EU countries. Pharmacies generally operate as single entities. Albania operates a flat markup schedule, with different markups for several classes of medicines. Wholesale and retail markups were decreased in April 2014. Regardless, wholesale markups remain high compared to EU 27. The extent to which the markup schedule is actually implemented requires further looking into and stricter control. VAT was until April 2014 charged on all medicines (both reimbursed and non reimbursed), but this is no longer the case. Retail markups do not appear to be excessive compared to EU 27.**

The MoH is in charge of calculating maximum prices for all prescription and expensive outpatient medicines, both reimbursed and non reimbursed(including OTC). International prices comparisons are undertaken by brand names, not INN, even for generic medicines. Countries taken into consideration are FYR Macedonia, Greece and Italy, the lowest published price being set as the Albanian price. Price comparisons to other Western Balkan countries reveal that Albania, particularly if its economic context is taken into consideration, has plenty potential to reduce prices of medicines. Medicines used in hospitals (inpatient) are procured by public tendering, however maximum prices are also determined by international price comparisons – following the same rules as for prescription medicines. The process of introducing new medicines to the lists of reimbursed medicines is not well defined. Managed entry agreements are not used to limit expenditure on expensive medicines.

Many generic companies operate in the Albanian pharmaceutical market and have their products reimbursed by the HIF. However, the current reimbursement system has so far not been able to incentivize or force them to compete on prices. For many of the reimbursed drugs there are multiple brand names in the market, and the difference between the lowest and highest retail price can be tenfold. This leads to unnecessarily high co-payments for patients as they commonly opt (as are recommended by their doctor or the pharmacist) to purchase the more expensive brands.

**The HIF does not engage in internal reference pricing (therapeutic value) of any sort. No mandatory price reduction rules exist for therapeutically similar me-too medicines. As no price comparisons by defined daily doses (DDD) are implemented even for the same International Nonproprietary Names (INN), substantial price differences appear in a large number of molecules if prices of different concentrations/strengths of same INNs are compared. In addition, the HIF overpays a substantial proportion of combination tablets and seems to be paying substantially different prices for defined daily doses of what other countries define as essentially similar (me too) medicines.**

INN prescribing is implemented and controlled by the HIF for reimbursed medicines only. Non reimbursed medicines can be prescribed by branded name. GPs do not attend peer groups, undergo visitations or engage in consultations with clinical pharmacologists regarding rational prescribing. The HIF issues indications/protocols for conditions that have to be met in order for GPs to prescribe medicines to individual patients. These are not listed in the formulary, but in a separate publication. The extent to which this is actually controlled remains unclear.The MoH and the HIF have as of yet not published official prescribing guidelines for expensive inpatient medicines that would take the cost effectiveness of the use of these products versus less expensive alternatives into account.

T**he list of reimbursed prescription medicines is fairly modest in most therapeutic areas, while it at the same time contains some expensive medicines not usually reimbursed in other Western Balkans countries. The cost effectiveness of the use of these medicines in Albanian financial circumstances is questionable. Contrary to the list of prescription medicines and expensive outpatient medicines, the list of hospital medicines is fairly rich in therapeutic options (including high priced medicines) – substantially richer than could be expected having in mind modest public expenditure on health. However, quantities of procured unit doses of expensive medicines are very low, far lower than could be expected if the numbers of patients treated is taken into consideration. Drug shortages occur on regular basis and available medicines are rationed using no clear resource allocation methodology. Instead, some patients appear to be instructed to procure therapy on their own.**

The MoH plans to introduce Track and trace technology and ePrescriptions.This should protect the system from counterfeit medicines and should prevent fraudulent behavior when medicines are charged to the HIF for phantom patients and later resold in the private market.

A set of regulatory measures targeting both the supply and demand sidesof the market should be implemented in order to:

1. Generate savings and ensure value-for-money for public health expenditures on medicines;
2. Enable the HIF to control the growth of expenditure on medicines;
3. Reduce very high rates of copayments for medicines through financial stimuli and administrative measures;
4. Increase the quality, effectiveness and transparency of reimbursement decision making;
5. Improve access and coverage for lifesaving medicines and
6. Promote rational prescribing of medicines

Recommendations have been marked as short/medium/long term depending on time required for implementation – having in mind available resources in Albania. Albanian authorities should be able to implement the majority in the short term with current human resources and some additional technical assistance. Some would however entail additional analyses, investments in IT and substantial human resources development.

|  |  |  |  |
| --- | --- | --- | --- |
| **Recommendations in short** | **Short Term (1-3 months)** | **Medium Term (6-12 months)** | **Long Term (12 months +)** |
| ***Supply-side policies*** |
| List packs instead of unit doses | ✗ |  |  |
| IRP - compare prices of off-patent medicines by INN, not brand name | ✗ |  |  |
| IRP - compare wholesale prices, not CFR | ✗ |  |  |
| IRP - expand the list of comparator countries to include Serbia and calculate prices twice annually | ✗ |  |  |
| IRP - implement price comparisons through an IT system |  |  | ✗ |
| Redefine the reimbursement decision making methodology and due process in more detail for prescription medicines and expensive outpatient medicines  | ✗ |  |  |
| Define the reimbursement decision making methodology and due process for hospital medicines | ✗ |  |  |
| Invest in building resources for HTA |  |  | ✗ |
| Introducelarger mandatory reimbursement price cuts for generic medicines that seek reimbursement  | ✗ |  |  |
| Introduce mandatory reimbursement price cuts for me too medicines that seek reimbursement  | ✗ |  |  |
| Reference price various strengths of INNs | ✗ |  |  |
| Reference price combination tablets vs individual components | ✗ |  |  |
| Reference price me too medicines in selected groups at ATC level 4 | ✗ |  |  |
| Update the reimbursement list quarterly |  | ✗ |  |
| Tender selected groups of prescription medicines  |  | ✗ | ✗ |
| Introduce mandatory managed entry agreements for all expensive medicines – both prescription and hospital and stop tendering patented hospital medicines  |  | ✗ |  |
| Introduce cross product agreements for reimbursement of new medicines  |  | ✗ |  |
|  |  |  |  |
| ***Demand side policies*** |
| Regulate promotion conducted by pharmaceutical companies  |  | ✗ |  |
| Educate prescribers on rational use of medicines  |  |  | ✗ |
| Benchmark GPs according to prescription indicators |  |  | ✗ |
| Introduce stricter control on adherence to prescribing guidelines for GPs  |  |  | ✗ |
| Prohibit specialists from recommending medicines using brand names and prescribing expensive hospital outpatient medicines by brand name and specialists and GPs from prescribing non reimbursed medicines by brand names  | ✗ |  |  |
| Introduce clinical guidelines for expensive inpatient and outpatient hospital medicines  |  |  | ✗ |
| Introduce regressive markups for prescription medicines and allow substitution of medicines prescribed by brand name only for a lower priced generic copy |  | ✗ |  |
| Implement public campaigns to assure patients of the quality of registered generics  | ✗ |  |  |
| Limit co-payments for reimbursed medicines | ✗ |  |  |
| ImplementePrescriptions and Track and Trace technology |  |  | ✗ |
| Expand the categories of Insured relieved of contributions to include financially deprived who can't afford copayments for all medicines or for a subset of essential medicines |  | ✗ |  |

# Background and overview

## Medicines in the Context of the Albanian Health Care System

Albania spends 6 percent of GDP on health care**[[1]](#footnote-2)**. In 2013, public spending on health was only 2.6 percent of GDP (43 percent), the lowest among countries in the region. Compared to other Western Balkans countries, total expenditure on health per capita in US$ is modest, as is the share of the government’s expenditure on health out of the total government expenditure. The share of private expenditure on health in total health expenditure is highest in the region (see table 1). Out of pocket expenditures are very high and account for as much as 55 percent of total expenditures on health. Of these, 45% are spent on pharmaceuticals, the remaining spent primarily on outpatient health services. Only 61 percent of the population is covered by social health insurance and up to 3 percent of households are pushed into poverty as a result of health spending. Unofficial payments remain common and are estimated at 10 percent of total out of pocket expenditure. Inpatient services and long-term treatment such as cancer, tuberculosis and multiple sclerosisare however (in theory)offered free of charge for the entire population[[2]](#footnote-3).

Table 1 – Albania compared to selected Western Balkans countries in macroeconomic context

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Country** | **Indicator** | **2009** | **2010** | **2011** | **2012** |
| **Albania** | **Health expenditure per capita (current US$)** | 229,99 | 206,62 | 242,92 | 227,51 |
| **Bulgaria** | 462,75 | 480,19 | 521,53 | 515,53 |
| **Croatia** | 1.095,20 | 1.050,69 | 991,82 | 908,31 |
| **Serbia** | 576,51 | 546,03 | 622,45 | 561,14 |
| **Albania** | **Health expenditure, private (% of total health expenditure)** | 52,91 | 54,61 | 52,06 | 52,40 |
| **Bulgaria** | 44,65 | 44,31 | 44,69 | 43,71 |
| **Croatia** | 15,11 | 15,20 | 17,51 | 17,68 |
| **Serbia** | 38,14 | 38,13 | 37,89 | 38,84 |
| **Albania** | **Health expenditure, public (% of government expenditure)** | 8,46 | 8,46 | 9,85 | 9,85 |
| **Bulgaria** | 9,65 | 11,28 | 11,28 | 11,76 |
| **Croatia** | 17,74 | 17,74 | 15,05 | 15,05 |
| **Serbia** | 13,92 | 14,08 | 14,09 | 13,36 |

Source: World Bank HNPSTATS database

Healthcare services are deliveredat three levels: i) primary healthcare which is provided by health centers and policlinics, ii) secondary healthcare provided at regional and districts hospitals and iii) tertiary care which remains quite limited mostly provided in Tirana[[3]](#footnote-4).

In terms of regulation, jurisdiction mainly falls under the Ministry of Health (MoH). The MoH is the government body in charge of setting all policies and strategies targeting healthcare as well as coordinating all actors within the system. The Albanian Parliament approves the annual budget dedicated to healthcare. Funds are collected by the tax office and Ministry of Finance (salary contributions for health insurance and funds from general taxation) and are pooled at the Health Insurance Fund (HIF).Recent reforms have increased the role of the HIF (previously named the Health Insurance Institute). The HIF, which is an independent body accountable directly to the parliament, finances primary health care (including prescription medicines), and secondary and tertiary hospitals on a contractual basis.Regional and tertiary hospitals manage their line item budgets but plans are in operation to increase their level of managerial autonomy.

**Due to issues with quality of primary and secondary care, patients often bypass the primary care gatekeeping system and seek care directly in tertiary hospitals or turn to the private market. Only about half of Albanian doctors gave correct diagnosis and treatment in response to hypothetical patient vignettes for common conditions. Drug shortages in public facilities are common. Clinical guidelines for five common conditions were developed under the Health Sector Modernization Project, but the application of these guidelines in not currently monitored.Staffing patterns and education for clinical, nursing and support staff need to be adapted to international standards.**

**Public spending is dominated by hospital expenditureswith a disproportionate share going towards tertiary services. Financial discipline in the system is weak and has led to a chronic problem of hospital payment arrears, which in 2013 amounted to 4,5 billion LEK ($US45 million), the majority of which were attributable to the tertiary Mother Theresa national referral hospital (QendraSpitaloreUniversitare (QSUT)).**

Current IT systems do not allow the MOH, HIF, or facility managers and physicians to monitor the quality and efficiency of care. For the most part, regional hospitals and primary care are without modern, complete, hospital information systems.

While the traditional Mediterranean diet has been posited for a long time as a major explanation for Albania’s relatively good adult health indicators, eating habits have changed and the Global Burden of Disease Profile 2010cites dietary risks as the main population health risk factor in Albania, followedby high blood pressure and smoking habits. The latter are another major source of concern due to their severe (especially long-term) detrimental impact on health outcomes, and since there is evidence that smoking rates havebeen rising recently**[[4]](#footnote-5)**.The planned free nationwide population check-up for the age group 40-65 is a first step in increasing the responsiveness of the system to the new epidemiological profile, but needs to be followedup by continued treatment to those diagnosed with any major health problem.

**Low spending on health care (both in terms of total and public expenditure), high proportion of out of pocket spending and a remarkably low percentage of health insured in the population point to the fact that Albania has historically not considered investing in health care as a priority. It is reasonable to expect that a substantial proportion of ill Albanians are currently not properly diagnosed and receiving rationally prescribed therapy. Apart from economic hardship, quality of care issues may further influence compliance (and volume of dispensed medicines) in therapy for diagnosed patients.**

This, combined with the expected rise in the incidence and prevalence of NCDs, the planned free nationwide population check-up for the age group 40-65 and underdevelopment of IT systems for monitoring health care provision may generate substantial potential for escalating expenditure on medicines in the coming years.

## Pharmaceutical Market in Albania

The HIF’s reimbursement budget has increased steadily over the years. The 2013 HIF drug reimbursement budget was 60 million Euros, up from approximately 56 million in 2012 and 49 million in 2011. According to the HIF, 90% of the reimbursement budget was spent on individuals in exempt categories, who receive 100% reimbursement[[5]](#footnote-6). Several categories of insured (estimated by HIF at 45% of the total number) are not required to pay copayments. In instances when several generics are reimbursed this applies only for the cheapest generic. These include the retired, disabled, children 0-1 years, cancer patients, TB patients, orphans andthe blind. In addition, veterans and war invalids do not have to pay copayments for any drugs in the list. No medicines are free at the point of use to other Albanians (both insured and non insured).

These exempt categories likely contribute significantly to expenditures on the top 10 reimbursed drugs by value.These drugs comprise 35% of the reimbursement budget (and the top 20 comprise 47% of the budget). These are mostly drugs for chronic conditions and cancers[[6]](#footnote-7).

Theannual growth of HIF’s expenditure on medicines has from 2008-2012 been in the double digits:between 14 and 20% annually. Due to underlying factors mentioned above, it is reasonable to expect that this trend may likely continue in the future.

Table 2 – HIF’s expenditure on medicines from 2006 to 2012

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Albania/Year** | **2006** | **2007** | **2008** | **2009** | **2010** | **2011** | **2012** |
| **HIF drug expenditureinmillion Lek** | 3,619 | 3,494 | 4,216 | 4,856 | 5,927 | 6,883 | 7,880 |
| **Percentage growth** |  | -3.46% | 20.66% | 15.19% | 22.06% | 16.12% | 14.49% |

Source: HIF

HIF’s expenditure on medicines per capita displays substantial variation from 1,518 Lek to 5,178 Lek by region. This phenomenon cannot be reasonably explained by differences in the regional burden of disease but may be the result of several issues that deserve further looking into – variations in the proportion of insured by region, different standards (and quality!) of care or concentration of patients in some regions, particularly the country’s capital Tirana.

Table 3 - HIF’s expenditure on medicines per capita by regions

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **HIF drug exp per capita by region in LEK** | **2006** | **2007** | **2008** | **2009** | **2010** | **2011** | **2012** |
| **Berat** | 891 | 817 | 1,005 | 1,157 | 1,343 | 1,476 | 1,760 |
| **Diber** | 698 | 586 | 694 | 882 | 1,051 | 1,363 | 1,553 |
| **Durres** | 1,011 | 930 | 1,103 | 1,255 | 1,493 | 1,662 | 1,857 |
| **Elbasan** | 648 | 686 | 870 | 1,068 | 1,299 | 1,659 | 1,905 |
| **Fier** | 1,016 | 884 | 1,026 | 1,139 | 1,271 | 1,471 | 1,665 |
| **Gjirokaster** | 666 | 658 | 835 | 1,021 | 1,286 | 1,628 | 1,973 |
| **Korce** | 962 | 914 | 1,066 | 1,267 | 1,553 | 1,824 | 2,126 |
| **Kukes** | 839 | 779 | 897 | 1,038 | 1,177 | 1,346 | 1,518 |
| **Lezhe** | 754 | 762 | 896 | 1,096 | 1,383 | 1,645 | 1,854 |
| **Shkoder** | 1,044 | 954 | 1,120 | 1,315 | 1,617 | 2,053 | 2,435 |
| **Tirana** | 2,310 | 2,322 | 2,841 | 3,212 | 4,028 | 4,548 | 5,178 |
| **Vlore** | 1,078 | 1,034 | 1,236 | 1,429 | 1,667 | 1,995 | 2,348 |

Source: HIF&Instat

Albania imports most of its drugs, however there are a few domestic manufacturers that produce a number of essential drugs[[7]](#footnote-8). According to the MoH, around 50 market authorization holders and 30 wholesalers operate in the pharmaceutical market. The number of wholesaler seems fairly high having in mind both the size of the population and the market, when compared to most western EU countries. Out of a total of 1600 pharmacies in Albania, 986 are contracted by the HIF to dispense reimbursed medicines. Pharmacies generally operate as single entities. Several pharmacy chains are also present in the market, the largest being FarmaNet Albania.

For many of the reimbursed drugs there are multiple brand names in the market, and the difference between the lowest and highest retail price can be seventeen fold.This leads to unnecessarily high co-payments for patients as they commonly opt (as are recommended by their doctor or the pharmacist) to purchase the more expensive brands.

Albania operates a flat markup schedule, with different markups for several classes of medicines. The extent to which the markup schedule is actually implemented requires further looking into and stricter control. The director of the National Center for Drug control reported instances in which drugs were sold to wholesalers at prices far lower than the declared/regulated CIF price (up to 69% discounts for metronidazole) – which would suggest that distributors engage in promotional actions to encourage dispensing of more expensive medicines.

Table 4 – Albanian markup schedule for medicines

|  |  |  |
| --- | --- | --- |
|  | **Markups before April 2014** | **Markups after April 2014** |
|  | **Wholesale markup** | **Retail pharmacy markup** | **Wholesale markup** | **Retail pharmacy markup** |
| **High price, supply-controlled drugs (for hospital use only)[[8]](#footnote-9)** | 6% | -- | 5% | -- |
| **High price drugs (outpatient)**  | 6% | 12% | 5,5% | -- |
| **Majority of drugs on reimbursement list** | 10% | 26% | 8% | 24% |
| **Drugs not on reimbursement list** | 14% | 29% | 11% | 25% |

VAT was until April 2014 charged on all medicines (both reimbursed and non reimbursed), but this is no longer the case. Wholesale and retail markups were decreased in April 2014. Regardless, wholesale markups remain high compared to EU 27.

Table 5[[9]](#footnote-10) - Average wholesale margins in EU countries

|  |  |
| --- | --- |
| **Country** | **Average Wholesale Margin/Year** |
| Austria  | 6,5-13,4% (2008) |
| Belgium | 8,45% (2007) |
| Bulgaria | 7-10% (2009) |
| Czech Republic | 4,3% (2007) |
| Denmark - unregulated | 6-7% (2009) |
| Finland - unregulated | 3% (2008) |
| France | 6,2% (2007) |
| Germany | 4-6,1% (2007) |
| Greece | 4% (2007) |
| Hungary | 6,04-6,36% (2007) |
| Italy | 3% (2010) |
| Latvia | 3,34% (2008) |
| Lithuania | 8-9% (2005) |
| Malta | 15% (2009) |
| Netherlands - unregulated | 13-24% (2007) |
| Poland | 9,78% (2007) |
| Portugal | 6,87% (2007) |
| Romania | 10-14% (2007) |
| Slovenia | 8-9% (2007) |
| Spain | 3,5% (2007) |
| Sweden - unregulated | 2-3% (2009) |

Retail markupsdo not appear to be excessive compared to EU 27 and afair number of smaller pharmacies have historically been known to run into bad debt[[10]](#footnote-11).

The National Center for Drug Control (NCDC) is in charge of marketing authorization and control of quality of medicines. The Commission on pricing and reimbursement set up at the MOH decides which drugs to include in the reimbursement list. Expenditures on reimbursed drugs are sustained by the HIF. The MoH’s pharmaceutical department is in charge of verifying prices declared by companies according to legislation by comparing them to reference countries. The Minister of Health approves the final list of reimbursed medicines.

# Pricing and Reimbursement of Medicines

## Pricing

The MoH is in charge of calculating maximum prices for all prescription and expensive outpatient medicines, both reimbursed and non reimbursed(including OTC) - totaling around 4000 active substances. International prices comparisons are undertaken by brand names, not INN, even for generic medicines. Countries taken into consideration are FYR Macedonia, Greece and Italy, the lowest published price being set as the Albanian price. If the price of a particular drug is not available in any of the three countries, the price of the drug in another country geographically close to Albania is taken into consideration. MoHdetermines the Cost Insurance and Freight (CIF)pricewhich is then enlarged by wholesale and retail markups to reach the finalAlbanianretailprice. MoH appears to be having issues in calculating CIF prices as back calculations from international retail and wholesale prices to CIF are not necessarily straightforward. These issues are then clarified and settled in negotiations. Prices of medicines produced in Albania are set through a negotiation procedure in which the ex-factory price is increased by 20%.

Companies are obliged to submit their price dossiers (detailing international prices) to the MoH’sPharmaceutical Department from September 1st until October 30th. The MoH pharmaceutical department in charge employs 6 staff who check the submitted dossiers. On December the 15th the MoH’sCommissionon Pricing and Reimbursement issues its price decisions based on the work of the department.

Companies can declare lower prices than calculated, but rarely do so. Last year MoH did not take into account low FYR Macedonian prices as the Macedonian website cited as the source in the relevant bylaw changed. No dedicated software is used for price comparisons.

Medicines used in hospitals (inpatient) are procured by public tendering, however maximum prices are also determined by international price comparisons – following the same rules as for prescription medicines.

## Reimbursement

Albania has two lists of reimbursed medicines: the prescription drug list thatincludesexpensive outpatient medicines and the hospital drug list. The HIF reimburses the list of prescription and expensive outpatient medicines.

The list of reimbursed prescription medicines is determined by the MoH’sCommissionon Pricing and Reimbursement.The commission is composed of representatives from the MOH, HIF, Ministry of Finance, NCDC, Faculty of Medicine and other external experts such as heads of hospital services.The list is updated once annually (last update in April 2014).No clear methodology or due process wereprovided for the decision making process regarding reimbursement of new molecules.

**During annual price recalculations that take part before the updating of the list, the HIF does not engage in internal reference pricing(therapeutic value) of any sort – even for different strengths of the same INN. Only the first generic that seeks reimbursementis required to reduce the reimbursed price by 20%. No mandatory price reduction rules exist for therapeutically similar me-too medicines either. This creates little incentive for companies to offer reduced reimbursed prices as medicines with higher copayments are commonly prescribed and dispensed.Managed entry agreements are not used to limit expenditure on expensive medicines. Tendering is not used for prescription drugs.**

The hospital list of medicines is determined annually by a commission set up at the department for hospital planning at the MOH.

**Previously, Albania used to have 2 hospital lists of medicines – one for the clinical hospital centreMother Teresa, and the other for all other hospitals. As of 2014, there is only one list. Until 2012 procurement of medicines was decentralized to individual hospitals, however for the last 2 years the MoH has been running centralized tenders. Hospitals submit desired products and needed quantities to the MoH. All drugs are tendered – patented and generic. According to the MoH, centralizing the tendering procedure did produce some savings, but more detailed analyses have not been undertaken. If more medicines are needed than tendered, hospitals can later on procure them individually, but should not pay more than the tendered price. While legally only Albanian wholesalers should be allowed to participate in tendering, in the last hospital tender published by the MOH “parallel trade” from Turkey and Greece was allowed in order to reduce prices. The effect of this measure remains to be evaluated as the tender is still not finalized.**

The process of introducing new medicines to the hospital inpatient list is not well defined. Heads of departments/hospital directors suggest which medicines should be included. Involvement of marketing authorization holders is not evident, neither is the methodology in which decisions on reimbursement are taken. TheMoH’s Commission then reviews these propositions, using no structured methodology. They appear to be mostly accepted. This is explained under the argument that the financial burden of introducing new medicines is borne by the hospitals themselves. No economic evaluation is undertaken by the MoH. The Hospital Directorate also participates in the process, primarily from the perspective of availability of budgeted funds, but again without documented due process.

One managed entry agreement appears to be in operation between Genzyme and Mother Teresa Clinical Hospital centre for Gaucher’s disease. Cerezyme is paid for 6 patients, while the company donates the drug for an additional 10. The HIF has so far not entered into any managed entry agreements for prescription nor expensive outpatient medicines.

# Prescribing and dispensing

INN prescribing is implemented and controlled by the HIF for reimbursed medicines only. Incompliant GPs can be financially punished, but it is not clear how fully is this regulation implemented. Non reimbursed medicines can be prescribed by branded name. GPs do not attend peer groups, undergo visitations or engage in consultations with clinical pharmacologists regarding rational prescribing. According to the HIF, GPs are however controlled and benchmarked according to expenditure on medicines based on the number of patients in care and their age structure. Good prescribers receive bonuses (1 extra salary every 6 months – this however depends on their performance on other performance indicatorsnot related to prescribing too).

The HIF issues indications/protocols for conditions that have to be met in order for GPs to prescribe medicines to individual patients. These are not listed in the formulary, but in a separate publication. The extent to which this is actually controlled remains unclear.

Table 6 provides a comparison of Albanian prescribing indications vs Croatian indications (for prescription medicines) and vs NICE/SMC guidelines for hospital (inpatient and outpatient) medicines.

Table 6 – indications for prescribing selected products, comparisons between Albania and Croatia or NICE (UK National Institute of Clinical Excellence)/SMC (Scottish Medicines Consortium) guidelines

|  |  |  |
| --- | --- | --- |
| **Medicine**  | **Albania** | **Croatia** |
| **Klopidogrel** | After coronary bypass or stent, up to 12 months | After coronary bypass or stent, up to 12 months |
| **Insulin glargin and detemir** | Only if other insulins proved unsuccessful in achieving normal glycamia | Only if other insulins proved unsuccessful in achieving normal glycamia |
| **Sartans** | Only for patients intolerant to ACE inhibitors after 2 months of therapy | Only for patients intolerant to ACE inhibitors after at least 4 months of therapy |
| **Statins** | It is recommended for primary prevention: dyslipidemia, hypercholesterolemia, type IIa ore mix type IIb. It is recommended to treat ischemia heart disease, diabetes ect. | Primary prevention after 3 months of diet if cholesterol is >7mmol/L and if patient is under 70 years of age |
| **Mircera** | For dialysis patients suffering from anemia with hemoglobin <90g/L. Also for patients who are not under dialysis treatment but with renal insufficiency <90g/L | For dialysis patients suffering from anemia with hemoglobin <90g/L |
| **Medicine**  | **Albania** | **NICE/ SMC** |
| **Xolair (omalizumab) for treatment of severe persistent confirmed allergic asthma** | *Adults and children older than 12 years old with severe persistent allergic asthma:*Positive in allergic tests of skin or in vitro reactivity against an aeroallergen Decline of pulmonary function (FEVI <80%)Frequent symptoms of severe Asthma despite high dosage daily treatment Frequent exacerbation of severe asthma despite high dosage daily treatment of inhaled corticosteroids, plus of a β2-agonist with a prolonged action.*Children between 6 and 12 years old with severe persistent allergic asthma and:*Positive in allergic tests of skin or in vitro reactivity against an aeroallergen Decline of pulmonary function (FEVI <80%)Frequent symptoms of severe Asthma despite high dosage daily treatment Frequent exacerbation of severe asthma despite high dosage daily treatment of inhaled corticosteroids, plus of a β2-agonist with a prolonged action. | Omalizumab[[11]](#footnote-12) is recommended as an option for treating severe persistent confirmed allergic IgE‑mediated asthma as an add‑on to optimised standard therapy in people aged 6 years and older: - who need continuous or frequent treatment with oral corticosteroids (defined as 4 or more courses in the previous year), and- only if the manufacturer makes omalizumab available with the discount agreed in the patient access scheme.Optimised standard therapy is defined as a full trial of and, if tolerated, documented compliance with inhaled high‑dose corticosteroids, long‑acting beta2 agonists, leukotriene receptor antagonists, theophyllines, oral corticosteroids, and smoking cessation if clinically appropriate. |
| **Glivec (imatinib) &Tasigna (nilotinib) for the first-line treatment of adults with chronic phase Philadelphia-chromosome-positive chronic myeloid leukaemia (CML** | Tasigna will be used only in adult patients who have been diagnosed with for the first time at the University Hospital Center “Mother Teresa” with chronic myeloid leukemia (positive chromosome Philadelphia bcr-abl positive) mainly at the chronic stage and also at an advanced stage. Tasigna will be used to treat adults diagnosed with chronic myeloid leukemia (positive chromosome Philadelphia bcr-abl positive) mainly at a chronic stage and also at an advanced stage when other treatments have failed. | Standard-dose imatinib[[12]](#footnote-13) (400 mg per day for patients in chronic phase) is recommended as an option for the first-line treatment of adults with chronic phase Philadelphia-chromosome-positive chronic myeloid leukaemia (CML).Nilotinib is recommended as an option for the first-line treatment of adults with chronic phase Philadelphia-chromosome-positive CML if the manufacturer makes nilotinib available with the discount agreed as part of the patient access scheme (PAS). |
| **Gilenya (fingolimod) for the treatment of multiple sclerosis** | Patients with multiple sclerosis (relapsing – remitting multiple sclerosis RRMS)Treatment should start within the first five years of the disease.The drug is recommended when there is no positive effect of treatment with interferon beta which has been utilized for at leas one year. Patients with MS that have at least one clinical relapse during treatment with interferon.Patients with no cardiac diseases, with normal balance of clinical and biochemical blood examination. The age of the patient for the first prescription should be 18-40 years old. | As single disease modifying therapy in highly active relapsing remitting multiple sclerosis (RRMS) for the following adult patient groups[[13]](#footnote-14): 1 Patients with high disease activity despite treatment with a beta-interferon.These patients may be defined as those who have failed to respond to a full and adequate course (normally at least one year of treatment) of beta-interferon. Patients should have had at least one relapse in the previous year while on therapy, and have at least nine T2-hyperintense lesions in cranial magnetic resonance imaging (MRI) or at least one gadolinium-enhancing lesion.A “non-responder” could also be defined as a patient with an unchanged or increased relapse rate or ongoing severe relapses, as compared to the previous year.orPatients with rapidly evolving severe RRMS defined by two or more disabling relapses in one year, and with one or more gadolinium enhancing lesions on brain MRI or a significant increase in T2 lesion load as compared to a previous recent MRI. SMC restriction: restricted to use as single disease modifying therapy in highly active RRMS in adult patients with high disease activity despite treatment with a beta-interferon with an unchanged or increased relapse rate or ongoing severe relapses, as compared to the previous year.  |
| **Avastin (bevacizumab) for the treatment of metastatic colorectal cancer** | 0 | NICE[[14]](#footnote-15) does not recommend bevacizumab in combination with oxaliplatin and either fluorouracil plus folinic acid or capecitabine for people with metastatic colorectal cancer. |
| **Alimta (pemetrexed) for the treatment of NSCLC and mesothelioma** | 0 | Pemetrexed[[15]](#footnote-16) in combination with cisplatin is recommended as an option for the first-line treatment of patients with locally advanced or metastatic non-small-cell lung cancer (NSCLC) only if the histology of the tumour has been confirmed as adenocarcinoma or large-cell carcinoma.Pemetrexed is not recommended for the maintenance treatment of locally advanced or metastatic non-squamous non-small-cell lung cancer in people whose disease has not progressed immediately following induction therapy with pemetrexed and cisplatin.Pemetrexed is recommended as a treatment option for malignant pleural mesothelioma only in people who have a World Health Organization (WHO) performance status of 0 or 1, who are considered to have advanced disease and for whom surgical resection is considered inappropriate. |
| **Velcade (bortezomib) for the treatment of multiple myeloma** | 0 | Bortezomib[[16]](#footnote-17)monotherapy is recommended as an option for the treatment of progressive multiple myeloma in people who are at first relapse having received one prior therapy and who have undergone, or are unsuitable for, bone marrow transplantation, under the following circumstances:-the response to bortezomib is measured using serum M protein after a maximum of four cycles of treatment, and treatment is continued only in people who have a complete or partial response (that is, reduction in serum M protein of 50% or more or, where serum M protein is not measurable, an appropriate alternative biochemical measure of response) and -the manufacturer rebates the full cost of bortezomib for people who, after a maximum of four cycles of treatment, have less than a partial response (as defined above). |

The MoH and the HIF have as of yet not published official prescribing guidelines for expensive inpatient medicines that would take the cost effectiveness of the use of these products versus less expensive alternativesinto account.Some work on clinical guidelines appears to have been undertaken several years ago. According to the chief pharmacist of the Mother Teresa Clinical Hospital, draft guidelines were prepared at the hospital and sent to the Ministry of Health but have since not been implemented. Tentatively, the reason for this was the unsustainable budget impact of guideline implementation as they implied wide use of very expensive products.

Although the use of expensive inpatient products is limited to the Tertiary Mother Teresa Clinical Hospital (which should imply some standardization in treatment protocols), the regulator should set clear rules for which patients the medicines should be used based not only on clinical merit, but also taking into consideration health economic arguments and availability of funding. Currently, the hospital procures very expensive products in quantities that are in no way sufficient to guarantee equal publicly funded therapy for all patients in need. Instead, drug shortages occur on regular basis and available medicines are rationed using no clear resource allocation methodology. Instead, some patients appear to be instructed to procure therapy on their own. Besides obvious ethical issues, this practice has both legal and practical problems. Pharmacies are by law not allowed to distribute hospital medicines packed in vials and the pharmaceutical cold chain can not be guaranteed if patients transport medicines on their own, thus potentially compromising their effectiveness.

Data on the regional hospitals’ expenditure on medicines could imply the same practice. Their total budgets for medicines increased from 339 million LEK in 2011 to 445 million in 2012, but were than administratively decreased by 40 million LEK (9%) in 2012. Data for the Tertiary Mother Teresa Clinical hospital was not available for analysis.

Table 7 – Regional hospitals’ expenditure on medicines from 2011-2013

|  |  |  |  |
| --- | --- | --- | --- |
| **Years/Regional hospital** | **2011** | **2012** | **2013** |
| **Berat** | 51.633.454,38  | 40.353.284,16 | 40.164.097,78 |
| **Durres** | 59.623.598,12 | 87.590.666,30 | 77.387.943,23 |
| **Elbasan** | 31.084.238,87 | 45.369.249,85 | 39.413.815,71 |
| **Fier** | 40.910.322,85 | 45.452.580,13 | 42.971.158,43 |
| **Gjirokaster** | 30.793.354,91 | 29.846.094,40 | 24.500.165,35 |
| **Kruje** | 7.897.141,17 | 7.250.905,21 | 6.073.129,53 |
| **Korce** | 37.897.120,17 | 74.536.703,54 | 51.349.923,97 |
| **Kukes** | 15.057.510,63 | 20.734.902,07 | 24.343.705,72 |
| **Lezhe** | 18.577.123,70 | 21.117.970,63 | 20.692.299,39 |
| **Shkoder** | 26.920.151,06 | 19.640.507,93 | 24.617.346,82 |
| **Vlore** | 19.165.021,49 | 53.719.409,75 | 53.577.011,30 |
| **Total** | **339.559.037,35**  | **445.612.273,97** | **405.090.597,23** |

**In addition, treatment could be rationalized. For instance, contrary to Albania and the majority of European countries, in England NICE does not recommend the use of Avastin for metastatic colorectal cancer as it judged that it does not provide enough benefit to patients to justify its high costs.**

**In general, most Albanian prescribing guidelines for prescription medicines and those for expensive outpatient medicines could be stricter or better defined. For instance, the HIF does not restrict statin prescribing while the Croatian Health Insurance Fund requires that for primary prevention statins can be prescribed only to patients with high cholesterol levels despite dieting and if they are aged under 70. In Albania, sartans can be prescribed for ACE inhibitor intolerant patients (caugh is the most common side effect) after 2 months of therapy, while in Croatia this period extends to 4 months to rule out seasonal respiratory diseases as a potential cause of caugh. In Albania, Xolair can be prescribed for treatment of severe persistent confirmed allergic asthma defined as for patients having frequent exacerbations of severe asthma despite high dosage daily treatment of inhaled corticosteroids, plus of a β2-agonist with a prolonged action, while NICE more clearly defines that it should be used for patients who need continuous or frequent treatment with oral corticosteroids (defined as 4 or more courses in the previous year), etc.**

**Very importantly (in particular if comparing cost of treatment and prices) NICE and SMC recommend the use of Xolair, Tasigna and many other expensive products only if providers do not pay the listed price, but if the manufacturer makes the products available with discounts agreed as part of patient access schemes (PAS).**

**Specialists cannot prescribe reimbursed medicines if patients seek reimbursement, but can recommend drugs by branded name. Specialist can prescribe non reimbursed drugs and expensive hospital outpatient medicines by brand name.**

Contracted pharmacies currently invoice the HIF in 48h after dispensing via an online IT system. Paper prescriptions are presented to the HIF every 2 weeks when these should be controlled/compared to what was prescribed. An estimated 3,5 million prescriptions are submitted every year so it is reasonable to expect that the controlling process is not exhaustive. Instead, random controls and controls of suspicious practices are controlled. The IT system validates certain data (preselection - no data can be input individually) such as number of insured individual, diagnosis, medicine, prescribing doctor, health centre, etc. The system automatically calculates the price of the pack, reimbursed amount and copayment. The system does not record which specialist suggested a certain medicine. All contracted pharmacies have PCs and are connected to the internet.

The process can be audited by HII’s Department of Pharmaceutical Control. Audits have been done by cross checking information that is sent electronically against paper copies of prescriptions. HIF analyses reimbursement trends from individual pharmacies and investigates / inspects pharmacies when there are suspicious fluctuations in reimbursement amounts. For example, in the past several months, HIF has inspected 30 pharmacies and imposed penalties for issues such as claims submitted for phantom patients, pharmacies holding on to patients' cards and using them to fill multiple prescriptions, and rural pharmacies that are not contracted with HII colluding with contracted urban-based pharmacies to claim reimbursements[[17]](#footnote-18).

# IT: ePrescriptions and Track & Trace Technology

Currently only a part of the GPs have PCs and internet connections (caring approximately for 50% of the population). All pharmacies contracted by the HIF have PCs and internet connections.

The HIF applied for an Italian government grant to introduce a pilot project for e-prescriptions in the Durres region. Results should be known in May.

Plans for the pilot are as of yet not definite. Several scenarios are considered:

* for the system to handle all prescriptions (both reimbursed and non reimbursed), this would however entail all pharmacies to be connected to the fund via internet as those not contracted are currently not.
* Clinical guidelines should be included, drug interactions, etc.

The MoH plans to introduce Track and trace technology by the end of the year. Two scenarios are currently under consideration – marking the packs at the border (customs) and marking the packs at production sites. This should protect the system from counterfeit medicines and should prevent fraudulent behavior when medicines are charged to the HIF for phantom patients and later resold in the private market.

# Review of Formulary Content, Prices and Expenditure

## Prescription Medicines& Expensive Outpatient Medicines

### List of reimbursed medicines – data and prices

The Albanian list of reimbursed medicines contains the following data for each entry: HIF reimbursement number, ATC code, INN and strength of unite dose, pharmaceutical form, brand name, market authorization holder, total price, copayment and reimbursed price. The formulary does not list packs nor their prices.

Table 8 – Data contained in the Albanian list of reimbursed prescription medicines

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **HIF No** | **ATC** | **INN** | **Form** | **Brand name** | **MAH** | **Total price**  | **Co-payment** | **Reimbursed price** |
| 2/105 | A02BA02 | Ranitidine 150 mg | f.c.tabl. | Ranitidine | Profarma | 3,3 | 1,0 | 2,3 |
| 2/16 | A02BA02 | Ranitidine 150 mg | f.c.tabl. | Raniberl | Berlin Chemie | 22,7 | 20,4 | 2,3 |

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 4/110 | A02BC01 | Omeprazole 20 mg | Caps. | Remeprazole 20 | Remedica | 14,8 | 4,4 | 10,4 |
| 4/7 | A02BC01 | Omeprazole 20 mg | Caps. | Eselan | Anfarm Hellas | 79,1 | 68,7 | 10,4 |

**The reimbursed price is derived by multiplying the price of the unit dose (if several generics exist- that of the cheapest one) by a factordetermined by the MoH’s committee on medicines that depends on the therapeutic area for which the medicine is used. However, market availability of the product is not taken into consideration, so it remains unclear whether these are actually always accessible to the public. In addition, the HIF does not benefit from the fact that in other countries unit doses in larger packs cost less than they do when packaged in smaller packs. The reimbursed price of the pack and the copayment are calculated during dispensing as prices of unit doses are multiplied by their number in the pack.**

Table 9 lists the reimbursement levels for selected therapeutic subgroups. In some, the level of reimbursement varies by molecule.

Table 9 – Reimbursement levels for selected therapeutic subgroups

|  |  |
| --- | --- |
| **Therapeutic subgroup**  | **Level of reimbursement** |
| Antacids (A02) | 70% |
| Drugs used in diabetes (A10) | 95% |
| Antithrombotic agents (B01) | 85% |
| Diuretics (C03) | 65% |
| Beta blocking agents (C07) | 60% |
| Calcium channel blockers (C08)amlodipinefelodipinenifedipine, verapamil, diltiazem | 85%50%80% |
| Antineoplastic and immunomodulating agents (L04) | 100% |
| Analgesics (N02) | 100% |
| Antiepileptics (N03) | 85% |
| Psycholeptics (N05)olanzapine | 80%50% |
| Etc. |  |

### Reimbursed medicines- therapeutic options

The list is fairly modest in most therapeutic areas. It does not contain a number of medicines reimbursed in other countries of the Western Balkans region. Table 10 lists some of the less expensive medicines typically reimbursed in other Western Balkans countries, but not reimbursed in Albania.

Table 10 – Medicines reimbursed in other Western Balkans countries not reimbursed in Albania

|  |  |
| --- | --- |
| **Therapeutic subgroup**  | **Medicines not reimbursed in Albania** |
| Antacids (A02) | famotidine, pantoprasole, lansoprasole and esomeprasole |
| Antiemetics and antinauseants (A04) | ondasentron, granisentron |
| Drugs for constipation (A06) | Lactulose |
| Drugs used in diabetes (A10) | Glimepiride |
| Antihypertensives (C02) | Doxazosin |
| Agents acting on the renin-angiotensin system (C09) | lisinopril and ramipril |
| Psycholeptics (N05) | bromazepam, alprazolam, nitrazepamandzolpidem |
| Psychoanaleptics (N06) | sertralin, paroxetin, escitalopram |
| Antiprotozoals (P01) | Metronidazol |
| Drugs for obstructive airway diseases (R03) | Montelukast |
| Etc. |

Including these (and others) in reimbursement would not necessarily incur substantial additional costs as they are in most cases essentially therapeutically similar (me-too medicines) to already reimbursed medicines, but would enrich therapeutic options for doctors. Many countries take advantage of including these in reimbursement by regulating that prices (reimbursed and total) have to be lower compared to similar already reimbursed medicines. In this way, through market competition and/or internal (therapeutic value) reference pricing, the reimbursed price of all subgroup medicines can be lowered.

At the same time the list contains some expensive medicines not usually reimbursed in other Western Balkans countries such as Concerta which is used to treat Attention Deficit Hyperactivity Disorder, Gilenya which is used to treat relapsing forms of Multiple Sclerosis, etc. The cost effectiveness of the use of these medicines in Albanian financial circumstances is questionable.

### Value for Money

#### Copayments

Many generic companies operate in the Albanian pharmaceutical market and have their products reimbursed by the HIF. However, the current reimbursement system has so far not been able to incentivize or force them to compete on prices. Table 9 lists several examples of a phenomenon that can be seen in virtually all therapeutic groups – copayments for the same drug varying up to 17 times (for risperidone). As bioequivalence and quality are assured by the National Center for Drug Control – patients spend out of pocket unnecessarily. The same applies to the HIF as for veterans and war invalids all versions can be prescribed with no copayments.

In most cases, originator products are more expensive and have higher copayments than generic copies. This phenomenon is frequent in many countries (albeit not nearly to such a degree) as originator companies defend profits when volumes decline by keeping prices high counting on brand loyal customers. However, in a number of INNs, generics have substantially higher copayments than originators. For instance, the copayment for a 50 mg tablet of bicalutamideproduced by Accord Healthcare is 2,3 times higher than for AstraZeneca’s originator Casodexproduct. The same applies for Roche’s Xeloda that has no copayment, while it’s generic copy produced by Alvogen retails at a copayment of 150,40 LEK per tablet.

Table 11 – Differences in copayments for selected prescription medicines

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **INN** | **Form** | **Brand name** | **MAH** | **Total price**  | **Co-payment** | **Reimbursed price** |
| Ranitidine 150 mg | tbl | Ranitidine | Profarma | 3,3 | 1,0 | 2,3 |
| Ranitidine 150 mg | tbl | Raniberl | Berlin Chemie | 22,7 | 20,4 | 2,3 |
| Bicalutamide 50 mg | tbl | Casodex | Astra Zeneca | 192,3 | 0,0 | 192,3 |
| Bicalutamide 50 mg | tbl | Bicaluta… | Accord Healthcare | 446,6 | 254,3 | 192,3 |
| Ibuprofen 400 mg | tbl | Ibuprofen | Replekpharm | 5,8 | 2,0 | 3,8 |
| Ibuprofen 400 mg | tbl | Brufen | Abbott | 9,8 | 6,0 | 3,8 |
| Ibuprofen 400 mg | tbl | Eudorlin Extra | Berlin Chemie | 37,6 | 33,8 | 3,8 |
| Risperidone 2 mg | tbl | Risset | Pliva | 7,9 | 1,6 | 6,3 |
| Risperidone 2 mg | tbl | Rispolept | Janssen - Cilag | 119,1 | 112,8 | 6,3 |
| Capecitabin 150mg | tbl | Xeloda | Roche | 96,20 | 0 | 96,2 |
| Capecitabin 150mg | tbl | Xalvobin | Alvogen | 246,60 | 150,40 | 96,2 |

This could imply several improper behaviors in the system – financial stimuli for specialists who recommend specific products to patients as well asprescribers and dispensers and/or general lack of trust in the state’s capability to assure high quality products in the market. In either case, patients spend out of pocket unnecessarily. More expensive copies are commonly if not predominantly dispensed. Table 12 lists the HIF’s expenditure in 2013 in Lek on cheapest versions compared to expenditure on all INN of same concentration for selected widely used products.

Table 12 – HIF’s expenditure in 2013 in Lek on cheapest versions compared to expenditure on all INN of same concentration for selected widely used products

|  |  |  |  |
| --- | --- | --- | --- |
| Enalapril 20 mg | tabl. | Profarma | 41.943.774 |
| **All 20 mg enalaprils** |  | **95.809.179** |
|  |  |  |  |  |
| Irbesartan 150mg  | tabl. | Nobel Ilac | 4.116.736 |
| **All 150 mg ibersartans** |  | **29.602.079** |
|  |  |  |  |  |
| Irbesartan 300mg  | tabl. | Nobel Ilac | 6.989.960 |
| **All 300 mg ibersartans** |  | **31.115.870** |
|  |  |  |  |  |
| Hydrochlortiazid 25 mg | tabl. | Profarma | 72.384.293 |
| **All 25 mg hydochlortiazids** |  | **103.015.786** |
|  |  |  |  |  |
| Atorvastatin 10mg | tabl. | Nobel Ilac | 13.539 |
| **All 10mg atorvastatins** |  | **1.899.817** |
|  |  |  |  |  |
| AMLODIPINE 10 MG | tabl. | Profarma | 12.199.450 |
| **All 10 mg amlodipines** |  | **26.142.972** |
|  |  |  |  |  |
| AMLODIPINE 5 MG | tabl. | Bosnalijek | 387 |
| **All 5 mg amlodipines** |  | **6.176.051** |

#### Reimbursed prices for different concentrations of same INN

As no price comparisons by defined daily doses (DDD) are implemented even for the same International Nonproprietary Names (INN), substantial price differences appearina large number of molecules if prices of different concentrations/strengths of same INNs are compared.This is a direct result of the current price setting methodology based solely on negotiations during which international prices by brand are compared. Table 13 lists several examples.

Table 13 – Price comparisons of different concentrations of same INNs

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **INN** | **Form** | **Brand name** | **MAH** | **Total price**  | **Co-payment** | **Reimbursed price** |
| Metoprolol 50 mg | tbl | Acis | Mibe | 7,5 | 2,2 | 5,3 |
| Metoprolol 100 mg | tbl | Metoprolol | Profarma | 2,7 | 0,8 | 1,9 |
| Metoprolol 200 mg | tbl | Acis | Mibe | 28,2 | 8,5 | 19,7 |
| Bisoprolol 5 mg | tbl | Tensec | Hemofarm | 6,6 | 2,0 | 4,6 |
| Bisoprolol 10 mg | tbl | Tensec | Hemofarm | 7,5 | 2,2 | 5,3 |
| Valsartan 80 mg | tbl | Valsartan | Profarma | 5,0 | 2,5 | 2,5 |
| Valsartan 160 mg | tbl | Valsartan | SocidadeTecnico | 22,6 | 11,3 | 11,3 |

In the example of metoprolol (defined daily dose is 150 mg), it would appear that if the 100 mg concentration tablet produced by Profarma is prescribed, the HIF pays the DDD at a reimbursed price of 2,85 LEK while if the 200 mg tablet produced by Mibe is prescribed, it pays the DDD at a reimbursed price of 14,775 LEK – or 7 times higher. The same applies to the copayment. In other words, prescribing two 100 mg tablets compared to prescribing one 200 mg tablet would save the HIF 15,9 LEK or 80% of the reimbursed price.

The example of bisoprolol is interesting as both 5 mg and 10 mg tablets are produced by the same company – Hemofarm. Hemofarm’s packages of Tensec contain 30 tablets. 150 mg of bisoprolol costs the HIF 138 LEK if prescribed in 5 mg tablets and almost half - 79,5 LEK if prescribed in 10 mg tablets.

For 160 mg of valsartane, the HIF will pay 11,3 LEK if prescribed in 160 mg tablet, but will pay 5 LEK (2,26 times less) if prescribed in 80 mg tablets. Copayments paid are 5 LEK ad 11,3 LEK respectively.

Somedifferences in prices of units doses related to strength are normal as unit doses in smaller packs internationally tend to be more expensive than those in larger packs due to production costs. In addition, smaller doses are necessary for some patients and some tablets can be split in half and others can’t - so not all are interchangeable.

Regardless, the enormous differences in prices demonstrated in the examples clearly indicate that prices of many concentrations could be substantially reduced if reimbursement prices for different concentrations were price referenced.

A comparison ofcosts of the same amount of active substance dispensed in larger unit doses vs. smaller doses foronly two generics (metoprolol and valsartan)indicates the magnitude of potential savings if same INN concentrations were price referencedfor all substances:

* In 2013, the HIF paid 43820 Lek for 200 mg metoprolol tablets. If the same quantity of metoprolol had been dispensed in 100 mg tablets instead, the HIF would have saved a total of 35 056 Lek.
* In 2013, the HIF paid 53771040 Lek for 160 mg valsartan tablets. If the same amount of valsartan had been dispensed in 80 mg tablets instead, the HIF would have saved as much as 32 262 624 Lek.

#### Reimbursed Price for Combinations versus individual components

The HIF overpays a substantial proportion of combination tablets. This is also a direct result of the current price setting methodology based solely on negotiations during which international prices by brand are compared. Table 14 provides two examples. It compares the prices of combination tablets compared to prices paid for individual components.

Table 14 - Price comparisons of selected combination products

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **INN** | **Form** | **Brand name** | **MAH** | **Total price**  | **Co-payment** | **Reimbursed price** |
| Atorvastatin 10mg +amlodipine 10mg | tbl | Caduet | Pfizer | 66,3 | 33,2 | 33,1 |
| Atorvastatine 10mg | tbl | Ateroz | BilimIlac | 6,2 | 3,1 | 3,1 |
| Amlodipine 10mg | tbl | Amlodipine | Profarma | 1,9 | 0,3 | 1,6 |
| Valsartan 160 mg + amlodipine 5 mg | tbl | Exforge | Novartis | 150,4 | 75,2 | 75,2 |
| Valsartan 160 mg | tbl | Valsartan | SociedadeTecnico | 22,6 | 11,3 | 11,3 |
| Amlodipine 5 mg | tbl | Monovas | Mustafa Nevzat | 2,1 | 0,4 | 1,7 |

If prescribed individually, the reimbursed price of 10 mg atorvastatin and 10 mg amlodipine sums up to

4,7 LEK. If a combination medicine that contains exactly the same doses of atorvastatine and amlodipine is prescribed, the HIF will reimburse it at 33,1 LEK – 7 times higher. Copayment paid by the patient is 9,7 times higher.

If prescribed individually, the reimbursed price of 160 mg valsartan and 5 mg amlodipine sums up to 13 LEK. If a combination medicine that contains exactly the same doses of valsartan and amlodipine is prescribed, the HIF will reimburse it at 75,2 LEK – 5,78 times higher. Copayment paid by the patient is 6,42 times higher.

* In 2013, the HIF paid 57 223 896 Lek for Exforge tablets. If the same amount of valsartan and amlodipine had been dispensed individually, the HIF would have saved as much as 47 495 833Lek. Data on expenditure of Caduet was not available for analysis.

#### Reimbursed prices for me-too medicines

Therapeutic value referencing (jumbo clusters) is a common pricing regulation strategy in Central and Eastern Europe, although variable in the scope of products for which it is used, the composition of the clusters, the ATC level of clustering (varying from 3 to 4) and the methodologies used to calculate internal reference prices – price per DDD being the most common criterion. It is used in many countries such as Bulgaria, Croatia, Czech Republic, Estonia, Hungary, Latvia, FYR Macedonia, Poland, Romania, Serbia and Slovenia.

Therapeutic subgroups are usually relatively broadly defined as pharmaceuticals that produce the same or similar therapeutic effects in treating the same or similar conditions. The effect of price changes on the pharmaceutical total expenditure depends on the price (copayment) and cross elasticity of demand, i.e., on how the demand of a medicinal product changes when the price (copayment) of that product changes and when the copayment of a competing medicinal product changes. Normally, a rise in the product price leads to a decrease in the demand for the product, while a rise in the price of a competing product has the opposite effect.

When engaging in internal reference pricing, it is important to compare similar strengths related to DDD and similar packages as larger packages usually cost less to produce by unit dose.

The HIF seems to be paying substantially different prices for defined daily doses of what other countries define as essentially similar (me too) medicines. Tables 15 and 16 list several examples - reimbursed prices paid for beta blocking agents and sartans (ARBs).

Table 15 – Price comparisons of selected me too medicines; beta blocking agents

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **INN & strength** | **DDD** | **Reimbursed price** | **Price paid by HIF for DDD** | **Hypothetical referent price for DDD** | **Potential savings** |
| Bisoprolol 10mg | 10 mg | 5,3 LEK | 5,3 LEK | 5 LEK | 5,7% |
| Nebivolol 5mg | 5mg | 12,9 LEK | 12,9 LEK | 5 LEK | 61,2% |
| Carvedilol 25mg | 37,5 mg | 7,5 LEK | **5 LEK**  | **5 LEK** |  |

Table 16 - Price comparisons of selected me too medicines; ARBs

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **INN & strength** | **DDD** | **Reimbursed price** | **Price paid by HIF for DDD** | **Hypothetical referent pricefor DDD** | **Potential savings** |
| Losartan 50mg | 50 mg | 1,5 LEK | **1,5 LEK** | **1,5 LEK** |  |
| Valsartan 80mg | 80 mg | 2,5 LEK | 2,5 LEK | 1,5 LEK | 40% |
| Irbersartan 150mg | 150 mg | 11,9 LEK | 11,9 LEK | 1,5 LEK | 87,4% |
| Telmisartan40mg | 40 mg | 16,8 LEK | 16,8 LEK | 1,5 LEK | 91% |
| Olmesartan 20mg | 20 mg | 46,8 LEK | 46,8 LEK | 1,5 LEK | 96,7% |

Nebivolol is 2,58 times and bisoprolol 1,5 times more expensive than carvedilol. Differences are more remarkable in sartans (Angiotensin II antagonists). Valsartan is 1,67 times more expensive than losartan, irbersartan 7,93 times more expensive, telmisartan 11,2 times more expensive and olmesartan 31,2 times more expensive.

* In 2013 the HIF paid 55 214 604 Lek for 10 mg bisoprolol tablets and 37 620 494 Lek for 5 mg nebivolol tablets. Had beta blocking agents been price referenced, the HIF would have saved a total of 26 170 974 Lek only on 1 DDD equivalent concentrations.
* In 2013 the HIF paid 36 745 066 Lek for 80 mg valsartan tablets, 29 602 079 for 150 mg irbersartan tablets and 180 800 031 Lek for 20 mg olmesartan tablets. Data on expenditure of telmisartan was not available for analysis. Had sartans been price referenced according to the DDD price of losartan, the HIF would have saved a total of 215 403 873 Lek only on 1 DDD equivalent concentrations of valsartan, irebersartan and olmesartan.

#### Reducing reimbursed prices at ATC level 5

As the list of medicines is renewed and prices are calculated once annually, all generics of a certain concentration have the same reimbursement price. Table 17 provides an example, it lists the prices of 100 mcg/doze budesonide in nasal spray.

Table 17 – Prices of generic copies of 100 mcg/doze budesonide in nasal spray

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Brand name** | **MAH** | **Total price**  | **Co-payment** | **Reimbursed price** |
| Buderen | Rafarm | 864,3 | 172,9 | 691,4 |
| Resata | Rafarm | 911,3 | 219,9 | 691,4 |
| Talgan | Anfarm Hellas | 1127,3 | 435,9 | 691,4 |
| Esonide | Kleva SA | 1691 | 999,6 | 691,4 |

The reimbursed price of all is the same – 691,4 LEK. Price cuts demanded for reimbursement on new generics to the lists are implemented in most CEE countries, but they vary from country to country. The Hungarian Health Insurance Fund is most severe, it demands a 40% price cut from the first generic entry, 20% for the second, 10% for the third and an additional 5% for every subsequent.

If the Albanian HIF updated the list more often and requested the same as the Hungarian Health Insurance Fund, the reimbursed price of the first generic would have fallen to 414,8 LEK, that of the second to 331,9 LEK, that of the third to 298,7 LEK and that of the fourth to 283,8 LEK. During next year’s price recalculations, the reimbursed price of the lowest priced version present in the market could have been requested from all copies (internal reference pricing at ATC level 5) and the HIF’s expenditure on budesonide could have been reduced by up to 60%.

* In 2013, the HIF paid 5 251 996 Lek for 100 mcg/doze budesonide in nasal spray. Had the HIF implemented price cuts equivalent to the Hungarian Health Insurance Fund, a 3 151 196 savings could have been demanded from producers.

### Price comparisons to Croatia, Serbia and FYR Macedonia

Table 18 compares wholesale prices of 20 selected medicines between Albania, Croatia, Serbia and FYR Macedonia. Products were selected based on high unit price, internationally prescribed quantities (blockbusters) or potential for expenditure growth in the future. Serbia and FYR Macedonia were selected as comparator countries due to geographic vicinity and similarity of economic context. Croatia was selected based on geographic vicinity and due to the fact that it is the last country to have joined the European Union – which all mentioned countries aspire to. The latter has proven to be an important factor in the Croatian national pricing and reimbursement process. As a number of EU countries reference prices in all EU member states, companies have for some time been highly reluctant to reduce listed prices in Croatia. Furthermore, it should be noted that as Croatia widely implemented managed entry agreements and financial discounts and discounts in stock as early as 2009, Croatian published prices do not necessarily reflect what is actually being paid for. Additionally, the majority of pharmaceutical companies group former Yugoslavian republics and Albania as the Western Balkans/Adria region, which implies consolidated regional pricing strategies.

Exchange rates used:

Bank of Albania, 21 May 2014[[18]](#footnote-19); 1USD= 102,17 LEK

Croatian National Bank[[19]](#footnote-20), 21 May 2014; 1 USD= 5,54 HRK

Serbian National Bank[[20]](#footnote-21), 21 May, 2014; 1 USD= 84.46

Macedonian National Bank[[21]](#footnote-22), 21 May 2014; 1 USD=44,95 MKD

Methodology of calculation:

Retail margin (26%) deduced from the retail price to derive the Albanian wholesale price for prescription medicines.Expensive outpatient medicineshaveno retail margin in Albania. Croatian, Macedonian and Serbian prices do not contain VAT.

Out of the sample of 20 medicines, Diovan, RisperidalConsta and Gylenia produced by Novartis are the only medicine cheapest in Albania. Serbia and FYR Macedonia, however, do not reimburse neither. Other cheaper generic valsartans are reimbursed. All other medicines are cheaper in at least one of the three comparator countries – the majority substantially so. This implies that Albania, particularly if its economic context is taken into consideration, has plenty potential to reduce prices of medicines.

Table 18 – Price comparisons of selected products in Albania, Croatia, Serbia and Macedonia

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Albanian retail price** | **Albanian wholesale price (/1,26)** | **Croatian wholesale price** | **Serbian wholesale price** | **Macedonian wholesale price** |
| Insulin Glargine 100 UI/ml – 3ml; pre-filled pen; Lantus Solostar; Aventis  | 18,50  | 14,68 | 12,59 | 11,10 | 12,67 |
| Insulin Detemir 100 UI/ml – 3ml, pre-filled pen; LevemirFlexpen; Novo Nordisk | 17,53 | 13,91 | 13,47 | 12,41 | 12,99 |
| InsulineLispro 100 NJ.N/ml – 3ml; kwikpen; Humalog; Eli Lilly | 9,87 | 7,83 | 9,31 | 4,97 | 7,86 |
| Valsartan 160 mg tbl, Diovan, Novartis | 0,61 | 0,48 | 0,91 | - | - |
| Atorvastatin 10mg + amlodipine 10mg tbl; Caduet; Pfizer | 0,65 | 0,52 | 0,07 | - | - |
| Dutasteride 0,5 mg caps; Avodart; GlaxoSmithKline | 0,91 | 0,72 | 0,72 | 0,69 | 0,73 |
| Bicalutamide 50mg; tbl; Casodex; AstraZeneca | 1,88 | 1,49 | 1,79 | 0,89 (PhSwiss) | 0,82 |
| Fentanyl 50mcg/h; patch; Durogesic; Janssen-Cilag | 7,16 | 5,68 | 4,02 | 5,67 | - |
| Levatiracetam 500mg; tbl; Keppra; UCB | 1,92 | 1,52 | 0,83 | 1,09 | 0,78 |
| Risperidone 2mg; tbl; Rispolept; Janssen-Cilag | 1,17 | 0,93 | 0,67 | 0,37 | - |
| SalmeterolXinaofate + Fluticasone Propionate Micronised 50/250 mcg unit dose; SeretideDiskus; GlaxoSmithKline | 56,97 | 45,21 | 37,36 | 34,60 | 38,19 |
| Budesonide + FormoterolFumarateDihydrateturbohaler 320/9 mcg/60 doza; SymbicortTurbohaler; AstraZeneca | 55,20 | 43,80 | 49,16 | 43,36 | 45,60 |
| Travoprost 40mcg/ml -2,5 ml; eye drops; Travatan; Alcon | 29,35 | 23,29 | 17,50 | 12,73 | 15,61 |
| Methoxi Polyethylene Glycol – epoetin beta 50mcg/0,3 ml; prefilled siringe; Mircera; Roche | 127,49 | 127,49 | 113,67 | 98,68 | - |
| Somatropine12mg 36 Nj.N; prefilled pen; Genotropin; Pfizer | 326,44 | 326,44 | 241 | 238,30 | 336 |
| Tenofovir 245mg; tbl; Viread; Gilead | 12,14 | 12,14 | 12,17 | 11,80 | 10,36 |
| Imatinib 100mg; caps; Glivec; Novartis | 25,31 | 25,31 | 25,67 | 17,50 | 23,47 |
| Peginterferonalfa- 2a 180mcg/0,5 ml; prefilled pen; Pegasys; Roche | 231,80 | 231,80 | 227,33 | 195,30 | 244,19 |
| Risperidone 50mg; inj; Risperdal Consta, Janssen Cilag | 196,23 | 196,23 | 213,72 | 207,17 | 199,53 |
| Fingolimod 0,5mg; Gilenya; Novartis | 82,06 | 82,06 | 87,90 | - | - |

## Inpatient medicines

### List of reimbursed medicines – data and prices

The hospital list of medicines contains the following data for each entry: INN and strength of unite dose, pharmaceutical form, unit price, quantity of procured unit doses and total budget hypothecated for the particular medicine.

As the MoH tenders unit doses, and not packs, it benefits from companies being able to tender larger (proportionally cheaper) packs.

Table 19 lists 15 of the most expensive medicines in total expenditure in the hospital list of medicines, including prices and quantities procured in 2012.

Table 19 – 15 highest spending expensive hospital medicines in 2012

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **INN** | **Dose** |  **Price limit**  | **Budget in LEK** | **Quantities 2014** |
| Trastuzumab | 150 mg |  77,352  |  145,498,265  |  1,881  |
| Sodium Chloride | 0.9% - 500 ml |  80  |  74,961,166  |  941,927  |
| Sevofluran | 250 ml |  24,250  |  63,606,550  |  2,623  |
| Rituximab  | 500 mg/50ml |  168,835  |  41,026,804  |  243  |
| Cefazoline sodium | 1 gram |  104  |  39,449,018  |  378,877  |
| Enoxaparinum sodium | 4000 Ul - 0.4 ml |  521  |  36,536,629  |  70,177  |
| Glucose | 5% - 500 ml |  86  |  36,252,624  |  423,844  |
| Enoxaparinum sodium | 6000 Ul - 0.6 ml |  707  |  29,693,846  |  42,025  |
| Bortezomib |  3,5 mg |  140,988  |  28,197,613  |  200  |
| Sunitinib | 50 mg |  23,575  |  27,040,312  |  1,147  |
| Prednisolone | 25 mg/2ml |  167  |  26,923,779  |  160,835  |
| Dalteparin | 5000 IU - 0.2 ml |  443  |  26,153,749  |  59,000  |
| Etanercept | 50 mg |  34,486  |  24,140,043  |  700  |
| Sodium Chloride | 0.9% - 250 ml |  86  |  23,976,734  |  277,905  |
| Ceftriaxone | 1 gram |  193  |  19,687,903  |  101,810  |
| Dextrose+ intralipid | 1440 ml |  6,152  |  18,820,262  |  3,059  |

### Reimbursed medicines - therapeutic options

Contrary to the list of prescription medicines and expensive outpatient medicines, the list of hospital medicines is fairly rich in therapeutic options (including high priced medicines) – substantially richer than could be expected having in mind modest public expenditure on health. **However, quantities of procured unit doses of expensive medicines are very low, far lower than could be expected if the numbers of patients treated is taken into consideration. This would imply that therapy is not standardized, i.e. all patients not having access to the same levels of publicly financed medicines. While hospitals are allowed to procure additional quantities of medicines subject to available funds, information gathered during the mission to Albania suggest that patients in major part have to finance these out of pocket as drug shortages are common. Alternatively, this issue may be contributing to growing hospital arrears – particularly in the Tertiary Mother Teresa hospital where the most complicated patients are treated and accounts for the majority of expenditure on expensive medicines.**

**Therapy is not standardized. The hospital list does not mention treatment protocols, and there are no formal conditions when a particular drug should or may be administered (lines of treatment).**

Table 20 lists 15 of the most expensive medicines by unit price in the hospital list of medicines, including prices and quantities procured.

Table 20 – Expenditure on 15 most expensive hospital medicines in 2012

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **INN** | **Dose** |  **Price limit**  | **Budget in Lek** | **Quantities 2014** |
| Octreotide | 30 mg/2,5ml |  233,603  | 5,840,085  | 25  |
| Pemetrexed | 500 mg  |  205,279  | 2,463,349  | 12  |
| Rituximab  | 500 mg/50ml |  168,835  | 41,026,804  | 243  |
| Bevacizumab | 400mg/16ml |  163,628  | 12,108,490  | 74  |
| Bortezomib |  3,5 mg |  140,988  | 28,197,613  | 200  |
| Infliximab  | 100 mg |  112,617  | 1,801,876  | 16  |
| Adalimumab | 40 mg |  81,325  | 2,927,691  | 36  |
| Trastuzumab | 150 mg |  77,352  | 145,498,265  | 1,881  |
| Reteplase | 10 UI |  52,064  | 2,603,177  | 50  |
| Recombinant Factor IX  | 250UI |  42,716  | 3,417,317  | 80  |
| Topotecan | 4 mg |  37,188  | 185,941  | 5  |
| Etanercept | 50 mg |  34,486  | 24,140,043  | 700  |
| Gosereline | 10.8 mg |  32,070  | 1,763,831  | 55  |
| Rituximab  | 100mg/10ml |  31,982  | 2,558,551  | 80  |
| Amphotericine B | 50mg/20ml liposomale |  28,623  | 4,293,457  | 150  |

### Price comparisons to Croatia, Serbia and FYR Macedonia

Table 21 compares prices of 5 most expensive medicines from the hospital list between Albania, Croatia, Serbia and FYR Macedonia. Again, it should be noted that as Croatia widely implemented managed entry agreements and financial discounts and discounts in stock as early as 2009, Croatian published prices do not reflect what is actually being paid for.

Exchange rates used:

Bank of Albania, 21 May 2014[[22]](#footnote-23); 1USD= 102,17 LEK

Croatian National Bank[[23]](#footnote-24), 21 May 2014; 1 USD= 5,54 HRK

Serbian National Bank[[24]](#footnote-25), 21 May, 2014; 1 USD= 84.46

Macedonian National Bank[[25]](#footnote-26), 21 May 2014; 1 USD=44,95 MKD

Methodology of calculation:

Croatian, Macedonian and Serbian prices do not contain VAT.

Table 21 - Price comparisons of selected products in Albania, Croatia, Serbia and Macedonia

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **INN** | **Albanian tendered price in USD** | **Croatian wholesale price in USD** | **Serbian wholesale price in USD** | **Macedonian wholesale price in USD** |
| Octreotide 30 mg/2,5ml | 2286,41 | 1610,78 | 1392,50 | 1400 |
| Pemetrexed 500 mg | 2009,19 | 1740,88 | 1535,47 | 1014,43 |
| Rituximab 500 mg/50ml | 1652,49 | 1585,02 | 1388,18 | 1686,53 |
| Bevacizumab 400mg/16ml | 1601,52 | 1622,32 | 1386,77 | 1581,86 |
| Bortezomib 3,5 mg | 1379,94 | 1610,31 | 1365,75 | 1239,36 |

Similar to prescription and expensive outpatient medicines, all 5 are cheaper in at least one of the three comparator countries – pemetrexed and octreotide substantially.

Prices of generics were not compared as comparator countries also procure these in tenders and information on prices is not publicly available.

# Discussion and Recommendations

This report aims to propose an array of specific regulatory measures that can be implemented simplyand rapidly. Some will however require building additional capacity in Albanian regulators.

The aims that the regulatory measures aim to achieve are:

1. savings and value-for-money for public health expenditures on medicines;
2. enabling the HIF to control the growth of expenditure on medicines;
3. reducing very high rates of copayments for medicines through financial stimuli and administrative measures;
4. increasing the quality, effectiveness and transparency of reimbursement decision making;
5. improving access and coverage for lifesaving medicines and
6. ensuring rational prescribing of medicines

In order to achieve this very ambitious set of objectives, an array of both supply and demand side targeted measures should be implemented. Recommendations have been marked as short/medium/long term depending on time required for implementation – having in mind available resources in Albania. Albanian authorities should be able to implement the majority in the short term with current human resources and some additional technical assistance. Some would however entail additional analyses, investments in IT and substantial human resources development.

|  |  |  |  |
| --- | --- | --- | --- |
| **Recommendations in short**  | **Short Term (1-3 months)** | **Medium Term (6-12 months)** | **Long Term (12 months +)** |
| ***Supply-side policies*** |
| List packs instead of unit doses | ✗ |  |  |
| IRP - compare prices of off-patent medicines by INN, not brand name  | ✗ |  |  |
| IRP - compare wholesale prices, not CFR  | ✗ |  |  |
| IRP - expand the list of comparator countries to include Serbia and calculate prices twice annually | ✗ |  |  |
| IRP - implement price comparisons through an IT system |  |  | ✗ |
| Redefine the reimbursement decision making methodology and due process in more detail for prescription medicines and expensive outpatient medicines  | ✗ |  |  |
| Define the reimbursement decision making methodology and due process for hospital medicines | ✗ |  |  |
| Invest in building resources for HTA |  |  | ✗ |
| Introduce larger mandatory reimbursement price cuts for generic medicines that seek reimbursement  | ✗ |  |  |
| Introduce mandatory reimbursement price cuts for me too medicines that seek reimbursement  | ✗ |  |  |
| Reference price various strengths of INNs | ✗ |  |  |
| Reference price combination tablets vs individual components | ✗ |  |  |
| Reference price me too medicines in selected groups at ATC level 4 | ✗ |  |  |
| Update the reimbursement list quarterly |  | ✗ |  |
| Tender selected groups of prescription medicines  |  | ✗ | ✗ |
| Introduce mandatory managed entry agreements for all expensive medicines – both prescription and hospital and stop tendering patented hospital medicines  |  | ✗ |  |
| Introduce cross product agreements for reimbursement of new medicines  |  | ✗ |  |
|  |  |  |  |
| ***Demand side policies*** |
| Regulate promotion conducted by pharmaceutical companies  |  | ✗ |  |
| Educate prescribers on rational use of medicines  |  |  | ✗ |
| Benchmark GPs according to prescription indicators |  |  | ✗ |
| Introduce stricter control on adherence to prescribing guidelines for GPs  |  |  | ✗ |
| Prohibit specialists from recommending medicines using brand names and prescribing expensive hospital outpatient medicines by brand name and specialists and GPs from prescribing non reimbursed medicines by brand names  | ✗ |  |  |
| Introduce clinical guidelines for expensive inpatient and outpatient hospital medicines  |  |  | ✗ |
| Introduce regressive markups for prescription medicines and allow substitution of medicines prescribed by brand name only for a lower priced generic copy |  | ✗ |  |
| Implement public campaigns to assure patients of the quality of registered generics  | ✗ |  |  |
| Limit co-payments for reimbursed medicines | ✗ |  |  |
| Implement ePrescriptions and Track and Trace technology |  |  | ✗ |
| Expand the categories of Insured relieved of contributions to include financially deprived who can't afford copayments for all medicines or for a subset of essential medicines |  | ✗ |  |

## Pricing

1. **Consider listing packs, not unit doses**

Most countries list packs, rather than unit doses. This makes international price comparisons easier, more straightforward and allows the payer to benefit from the relatively lower price of unit doses in larger packs compared to those of smaller ones. Price differences appear due to costs of production. Larger packs are particularly suitable for patients suffering from chronic non communicable diseases who take their therapy continuously or in prolonged periods of time.

1. **Consider comparing prices of off-patent medicines by INN, not brand name**

Most countries compare prices of off-patent medicines by INN, not brand name. As patents expire and generic companies start to market copies, prices paid for the particular INN in most countries fall sharply as payers swiftly reduce the reimbursed price and generic producers compete on lowering copayments (if they exist). Several methodologies can be used to set the maximum national price – mean, median, lowest priced INN in other countries, average of the least several expensive copies, etc. Comparing international prices of off-patent medicines by brand name as is currently done in Albania is less effective in lowering prices. Originator companies rarely reduce prices to the levels of generic copies - trying to maximize profit through higher prices counting on brand loyalty from a subset of doctors and patients. Branded generics, common in the Western Balkans countries, can also be overpriced leading to unnecessarily high Albanian prices.

1. **Consider comparing wholesale prices, not CFR prices**

International price comparisons can be very complicated as medicines have a number of associated prices (ex factory, CFR, wholesale, retail, etc.) and as VAT rates on medicines vary by country. However, a lot of countries choose to compare wholesale prices as these:

1. fairly accurately reflect the value that a particular payer is paying for a pack of medicines delivered to the patient. The remaining additional cost (retail markup) can in this perspective be viewed as a national cost of having a wide net of pharmacies making therapy and advice accessible to the population.
2. Simplify comparisons as most other countries publish wholesale prices, or retail prices from which wholesale prices can be easily deduced as retail markups are publicly accessible information.

**The current Albanian practice of determining CFR prices through negotiations seems more complicated and less straightforward.**

1. **Consider expanding the list of comparator countries to include Serbia and calculating prices twice annually**

As was mentioned above, a number of CEE countries compare prices from more countries than Albania does. Expanding the list to other low priced countries and calculating prices twice annually to benefit from continuous price reductions in comparator countries could be a successful strategy in lowering Albanian prices that are comparably higher than what Croatia, Serbia and FYR Macedonia are paying, particularly having in mind Albania’s economic context. An alternative approach could be including a higher priced country with a wider set of reimbursed medicines, but reducing these for comparisons by a factor that would reflect the difference in GDP between the two countries.

1. **Consider implementing price comparisons through an IT system**

International price comparisons are complex to implement as prices of thousands of same and similar packs from several countries have to be compared immaculately. Implementing price comparisons through an IT system would reduce the possibility of error and corruption, enable swift calculations of future savings and document the entire administrative procedure. Switching international price comparisons to IT at the Croatian Health Insurance Fund reduced the length of the procedure, and increased its efficiency and transparency.

## Reimbursement

1. **Consider redefining the reimbursement decision making methodology and due process in more detail for prescription medicines and expensive outpatient medicines**(does not apply for generic copies of already reimbursed products where the application should be as simple as possible)

The current Albanian reimbursement due process and decision making methodology could be better defined. While it would not be rational to expect that a full blown health technology assessment process of the scope NICE (UK National Institute of Clinical Excellence) or SMC (Scottish Medicines Consortium) engage in can be easily and shortly developed and implemented, a lot can be improved in a very short while by better defining rules and documentation that companies have to submit when applying for reimbursement. The system should be made as transparent as possible – ideally applications and decisions should be published on the HIF’s website. Minimal required documentation could include:

* Albanian marketing authorization, the Summary of Product Characteristics and the Patient Information Leaflet;
* pharmacodynamic properties, pharmacokinetic properties, posology, adverse reactions and interactions, special remarks: contra-indications, pregnancy, lactation, influence on psychophysical abilities, administration in renal and hepatic insufficiency and in special age groups;
* calculation of the price in line with national legislation;
* scientific evidence demonstrating the advantages of the medicinal product for suggested indication(s) over the comparators, and primarily over medicinal products already included in the reimbursement list of the Health Insurance Fund; ideally meta-analysis or a systematic review of randomized controlled trials published in indexed professional and scientific journals or exceptionally at least one or more randomized controlled trials published in indexed professional and scientific journals
* description of the current clinical practice in Albania by indication for which the application has been submitted and for which medicinal products already included in the HIF’s lists are used, along with comments on efficacy and safety;
* description and analysis of the effect of the change of pharmacological therapy and the assessment of other changes in patient healthcare resulting from the inclusion of the medicinal product in the list (including the use of complementary products and services);
* a tabular comparative presentation of the price of the therapy with the medicinal product with the price of the therapy of the same indication with medicinal products included in the HIF’s reimbursement list for which an application has been submitted in the appropriate time interval (disease episode, annually, etc.);
* budget impact analysis on the HIF’s expenditure on medicines and the HIF’s overall expenditure prepared in line with ISPOR (International Society For Pharmacoeconomics and Outcomes Research) guidelines[[26]](#footnote-27);
* tabular presentation of the status in health insurance or healthcare system of all Member States of the European Union, including reimbursed indications, amount covered by the compulsory health insurance of each State, amount of surcharges and other information relevant for financing of the medicinal product in individual Member States;
* if available, a decision or opinion about financing of the medicinal product issued by the competent authority in England (NICE) and Scotland (SMC) engaged in the assessment of healthcare technology, along with indications and instructions for use;
* therapeutic guidelines of American and European expert associations for indications for which an application has been submitted;
* optionally, the applicant may also enclose a cost efficiency analysis;

Due process should be aligned to the European Union’s Transparency directive[[27]](#footnote-28)

1. **Consider defining the reimbursement decision making methodology and due process for hospital medicines**

The current system of reimbursing medicines used in hospitals should be fully aligned to the process suggested above for prescription medicines and expensive outpatient medicines in which pharmaceutical companies apply for reimbursement. The administration of both processes should be handled by a single organization and decision making should be handled by a single committee. Use of hospital medicines is highly interlinked to the use of prescription medicines and developing sufficient capacity to process the applications and reach quality decisions at two different institutions in a country the size of Albania may not be realistic.

1. **Considerinvesting in building resources for Health technology assessment (HTA)**

Health technology assessment (HTA) is the systematic evaluation of properties, effects, and/or impacts of health technology. Its main purpose is to inform technology-related policy-making in health care, and thus improve the uptake of cost-effective new technologies and prevent the uptake of technologies that are of doubtful value for the health system.Developing a full scale HTA system including staff able to evaluate cost effectiveness/utility analyses that would be submitted by industry requires substantial time and investment. In addition, detailed data on epidemiology, resources, clinical practice etc. should be publicly available so thatcompanies would be able to produce analyses. The above mentioned requires substantial time and investment in human resources.

For these reasons, in addition to investing in building resources as a mid term policy goal, in the short term Albania should consider taking into account HTAs produced in other countries. NICE and SMC publish their single and multiple technology assessments online. That said, comparisons should be made with great caution as prices, resources, clinical practice, etc. vary substantially between Albania and the UK. Nevertheless, if a high-income country finds that a particular health technology is not cost-effective, it is unlikely to be cost-effective in a low- and middle-income setting either[[28]](#footnote-29).

1. **Consider introducing larger mandatory reimbursement price cuts for generic medicines that seek reimbursement**

As was mentioned above, most CEE countries have introduced mandatory reimbursement price cuts for generic copies seeking reimbursement. This, combined with ATC level 5 internal reference pricing (already in use in Albania), is a powerful mechanisms for reducing reimbursed prices of medicines.

1. **Consider introducing mandatory reimbursement price cuts for me too medicines that seek reimbursement**

As was mentioned above, a large number of CEE countries reference price medicines according to therapeutic value. Similar to the mechanism proposed for generic medicines, the HIF could condition reimbursing products with same or similar therapeutic and pharmacological properties (me too medicines) to those already reimbursed on companies accepting lower reimbursement prices compared to already reimbursed competitors. This would lower the cost of treatment for illnesses that are already treated by reimbursed products.

1. **Consider reference pricing various strengths of INNs**

Having in mind the abundant substantial differences in prices of same strengths of single INNs (both in expected and absurd directions, i.e. greater strengths costing less than smaller strengths), the HIF should consider reference pricing various strengths of single INNs according to LEK per defined daily dose calculations. This data will serve as powerful arguments for price reducing negotiations with pharmaceutical companies. Having in mind the scale and presence of differences, fast and substantial savings could be made. A rule should be discussed on possibly establishing allowed percentage differences in LEK paid for DDDs for various strengths of different INNs. Prices in other countries should be analyzed for informed decision making.

1. **Consider reference pricing combination tablets**

The HIF should consider referencing reimbursed prices of combination tablets versus individual components. There are no rational reasons why combination tablets should be reimbursed at a higher level compared to individual components.

1. **Consider reference pricing me too medicines in selected groups at ATC level 4**

As discussed above, a number of CEE countries reference reimbursed prices of therapeutically similar medicines, in major part using relatively simple price per DDD calculations. The HIF should consider the same, at least for a limited number of high expenditure groups or groups that have high expenditure growth potential. It is important to note that similar strengths and packs should be compared between different INNs. Popular “jumbo groups” for internal price referencing include statins, beta blocking agents, sartans (ARBs), proton pump inhibitors, insulins, oral antidiabetics, diuretics, ACE inhibitors, antibiotics, etc.

1. **Consider updating the reimbursement list quarterly**

More regular updating of the list would broaden therapeutic options for doctors and patients, but would also speed the positive price effects of proposed price reducing measures.

1. **Consider tendering selected groups of prescription medicines**

An alternative to ATC level 5 reference pricing may be tendering certain high expenditure groups of medicines that have plenty registered generic variants in Albania in order to guarantee market competition. Whereas tendering procedures are widely used in the hospital sector, in the last couple of years they are also being rolled out in ambulatory care in an increasing number of European countries with a view to constraining pharmaceutical expenditure.

Significant short term pharmaceutical budget savings can be achieved from tenders. However, sound financial guarantees have to be demanded from companies to ensure uninterrupted delivery of products. In addition, countries have had various experiences with tenders, for instance in Belgium tendering produced massive savings for simvastatin, but these savings were offset by the fact that physicians switched their prescribing patterns to medicines with a similar therapeutic indication that did not fall under the tendering procedure, so-called ‘re-allocation of demand’, and total expenditure actually increased[[29]](#footnote-30).Countries that have implemented tendering procedures have sometimes witnessed a decrease in pharmaceutical investments, a slowdown in the development of the generic medicine market, short-term absences of some medicines due to logistic shortages, a reduction in pharmacist remuneration, and problems with patient compliance[[30]](#footnote-31).

1. **Consider introducing mandatory managed entry agreements for all expensive medicines – both prescription and hospital and stop tendering patented hospital medicines**

Albania should consider introducing managed entry agreements. As was already discussed, formal arrangements between payers and manufacturers with the aim of sharing the financial risk due to uncertainty surrounding the introduction of new technologies have been developed and introduced in most European countries in order to enable access to new medicines and control expenditure. One of the consequences of these agreements established in other countries is that published prices that Albania takes into consideration during international price comparisons in effect overstate what they are really paying – leading to too high Albanian prices. These agreements can take different forms, including price-volume agreements (PVAs), financial discounts, discounts in goods, outcome guarantees, disease management programs, etc. A variety of names have been used to describe these schemes (e.g. risk-sharing agreements (RSAs), performance-based agreements (PBAs), patient access schemes (PAS), etc.), which have been recently summarized with the concept of “managed entry agreements (MEAs)”.

**It is unlikely that tendering patented hospital medicines will be effective in reducing prices. If only national distributors are allowed to compete, no market competition can be expected. Even if distributors from other countries are allowed to apply (parallel import), substantially better prices can be negotiated through managed entry agreements.**

1. **Consider introducing cross product agreements for reimbursement of new medicines**

Albania should consider allowing companies to submit binding offers where the application which refers to a medicine considered by the HIF for reimbursement is connected with a parallel application for the reduction of a price of an already reimbursed medicine. In this way, new therapies can be introduced without additional costs.

## Prescribing

1. **Consider regulating promotion conducted by pharmaceutical companies**

Albania should consider regulating the relationship between pharmaceutical companies and doctors. The regulation should seek to ensure that pharmaceutical companies conduct promotion and interaction in a truthful manner, avoiding deceptive practices and potential conflicts of interest with healthcare professionals. Regulation should set fundamental rules and cover activities such as medicine advertising in medical publications, contacts with sales representatives and the supply of samples, gifts and hospitality. Mandatory collection of data on financial transactions, hospitality, gifts etc. should also be considered.

1. **Consider educating prescribers on rational use of medicines**

Albania should consider investing in education for prescribers on rational use of medicines. Rational use of medicines requires that "patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community". Irrational use of medicines is a major problem worldwide. WHO estimates that more than half of all medicines are prescribed, dispensed or sold inappropriately, and that half of all patients fail to take them correctly[[31]](#footnote-32). The overuse, underuse or misuse of medicines results in wastage of scarce resources and widespread health hazards. Peer groups, visitations, case reviews by clinical pharmacologists, etc. are most often forms in which rational use of medicines is promoted internationally.

1. **Consider benchmarking GPs according to prescription indicators**

Albania should consider benchmarking GPs according to prescription indicators for high spending groups of medicines and those that have high growth of expenditure potential. Possible indicators could include overall expenditure on groups of medicines or average cost by prescription (adjusted by number and age structure of patients), proportion of lowest copayment generic copies dispensed by pharmacists, ARBs as percentage of all renin-angiotensin prescriptions by volume, DDDs prescribed of hypnotics and anxiolytics per 1000 patients, low cost statins as percentage of all prescribed statins, etc.

1. **Consider introducing stricter control on adherence to prescribing guidelines for GPs**

While the HIF already publishes mandatory prescribing guidelines/protocols for reimbursed prescription medicines, it is unclear to what extent this is matter is actually controlled. Regional experience suggests that HIF staff usually lack knowledge and time for comprehensive control of prescribers. Focusing attention on high expenditure GPs and molecules should be considered, as well as appropriate financial punishments for non-abiding prescribers.

1. **Consider prohibiting specialists from recommending medicines using brand names and prescribing expensive hospital outpatient medicines by brand name and specialists and GPs from prescribing non reimbursed medicines by branded names**

Hospital specialists commonly recommend branded products to patients (GPs prescribe in INN, but pharmacists dispense according to the specialist’s recommendation) and prescribe expensive hospital outpatient medicines and non reimbursed medicines by branded name. The latter applies to GPs too. There is no rational reason why all prescribing and recommendations should not be in INN.

1. **Consider introducing clinical guidelines for expensive inpatient and outpatient hospital medicines**

Albania should consider introducing and promoting clinical guidelines for expensive medicines in order to ensure standardization and quality of therapy for all patients. Clinical guidelines are recommendations on the appropriate treatment and care of people with specific diseases and conditions. Clinical guidelines should be based on the best available evidence. Sense of ownership and adaptation to local circumstances (both economic and medical)are instrumental in ensuring adherence, so it is important to include national professional associations in the guideline creation process. International guidelines should definitely be consulted (NICE, European and American professional associations).

## Dispensing

1. **Consider introducing regressive markups for off patent prescription medicines and allowing substitution of medicines prescribed by brand name only for a lower priced generic copy**

The current 24% retail markup is stimulating pharmacists to dispense higher priced generic copies - the higher the total price of the medicine, the higher the markup for the pharmacists. In this way the HIF does not spend more as reimbursed prices are the same for all copies, but patients pay higher copayments. Albania should consider introducing a markup scale for prescription medicines including higher retail markups for less expensive copies and lower markups for more expensive copies that would financially stimulate pharmacists to dispense more affordable products. Switching from prescribed branded name should also be allowedbut only for a cheaper copy. Implementation of this measure would not require any additional resources from the HIF as it is budget neutral.

## Educating patients

1. **Consider public campaigns to assure patients of the quality of registered generics**

Having in mind excessive consumption on copayments for overpriced originators (and too expensive generic versions), Albania should consider funding a promotional campaign that would assure the population of the quality of all medicines registered in the Albanian market – controlled by the National Centre for Drug Control.

## Copayments

1. **Consider limiting copayments for reimbursed medicines**

In other countries of the region, pharmaceutical producers of generics compete on price more aggressively. This leads to smaller copayments for patients. This is not the case in Albania where many instances exist where copayments for certain generics/ originator products exceed over tenfold copayments on other reimbursed versions of the same INN. Albania should consider protecting its population from unnecessary expenditure by limiting copayments for medicines that seek reimbursement to a certain proportion of the least copayment of a reimbursed copy of the INN.

## IT

1. **Continue implementing ePrescriptions and Track and trace technology**

Albania is set on implementing ePrescriptions and Track and trace technology for medicines. Both should be implemented as they will allow for far more timely and sophisticated control of the market, prevention of fraud, circulation of counterfeit medicines, etc.

## Access

1. **Consider expanding the categories of insured relieved of contributions to include financially deprived who can’t afford copayments for all medicines or for a subset of essential medicines**

Copayments have internationally been proven to interfere with therapy compliance for financially deprived individuals[[32]](#footnote-33). Depending on financial circumstances and having in mind very low public expenditure on healthcare, Albania should consider expanding the categories of insured relieved of copayments to include financially deprived individuals who can’t afford them – either for all medicines or for a subset of essential medicines.The additional short term cost could be offset by the implementation of a number of price reducing measures proposed in this report.

The World Health Organization updates its list of essential medicines once every two years[[33]](#footnote-34). Its core listpresents a list of minimum medicine needs for a basic health‐care system, listing the most efficacious, safe and cost‐effective medicines for priority conditions. Priority conditions are selected on the basis of current and estimated future public health relevance, and potential for safe and cost‐effective treatment. Its complementary list presents essential medicines for priority diseases, for which specialized diagnostic or monitoring facilities, and/or specialist medical care, and/or specialist training are needed. In case of doubt medicines may also be listed as complementary on the basis of consistent higher costs or less attractive cost-effectiveness in a variety of settings.

Depending on the choice of treatments to be free at the point of use, mid term and long term costs for the HIF could actually be substantially decreased due to avoiding costly complications of most NCDs that arise if patients are not treated. This in particular applies to diseases such as hypertension, cardiovascular disease, high cholesterol levels, diabetes, etc.

# Appendix 1 - Overview of pharmaceutical policies in CEE of interest for Albania

Pricing and reimbursement of medicines in CEE is deeply influenced by policies implemented and developed in western EU member states. The region is composed of “new” EU member states, candidate countries and aspiring candidates. Thus, pricing and reimbursement systems in CEE have many common elements both to each other and to western EU countries. Implementation of these measures requires arangeofskillsandcapacities in order to be successful, such as a sound legal basis, political will, enforcementcapacity,managementskillsandsystemsto collect data for measuring both the baseline and impact of a given measure. However, as CEE countries generally have underdeveloped governance and management systems in the public sector, these have had variable success in restraining the growth of expenditure on medicines.

Although the EU’s Transparency directive (EU 89/195) stipulates basic rules in pricing and reimbursement procedures, member states can largely formulate policies independently. Recent European Commission's initiatives in the field of pricing and reimbursement seek to foster cooperation through the establishment of a structured dialogue between the competent national authorities and all relevant stakeholders. The core objective is not only to enhance the functioning of the Internal Market, but also to ensure that national systems achieve an adequate balance between cost-containment, pharmaceutical innovation and patients' access to medicines. Nevertheless, in CEE the focus has been mostly on cost containment.

**External reference pricing**

External reference pricing (ERP), also known as international price comparisons, has become one of the most common cost-containment tools to reduce prices for in-patent pharmaceuticals in the EU member states. ERP is also applied worldwide with EU member states often used as reference countries by non-EU countries (e.g. Brazil, Jordan, South Africa, Japan, Turkey, Canada, and Australia).

All European countries except the UK and Sweden (expected to reintroduce it in 2014!) apply international price comparisons either as the main systematic criterion or as a supportive argument for price negotiations[[34]](#footnote-35). The CEE region follows suit. External price referencing is one the main criteria used for initial price setting for new medicines in most CEE countries under consideration for reimbursement and is regularly used for price recalculations of marketed products that are undertaken in various time cycles. Montenegro and Kosovo are the only exceptions. Countries predominantly regulate only the prices of reimbursed products.

When the pharmaceutical formulation of a drug in the reference country is different from the formulation approved in the referencing country, some countries do not take into account the different formulation for ERP (e.g. Latvia, Slovakia), while other countries (Croatia, Slovenia, Hungary, etc.) consider the different pharmaceutical formulation only if it is similar to the one approved (e.g. oral solid forms such as capsule versus tablet can be compared to each other but not to injectable forms).

Bosnia and Herzegovinaconsults prices in Slovenia, Croatia and Serbia. If prices are not available in any of these, Austrian and Italian prices are taken into account. For new medicines seeking reimbursement, the regulator requires a discount at a variable rate from 0 to 10% from the average listed price in referenced countries. For reimbursed products, annual recalculation rules require lowering the prices to the same levels as described for medicines seeking reimbursement.

In Bulgaria, the price proposed by the manufacturer cannot exceed the equivalent of the lowest producer price of a drug on the reference markets of Denmark, Estonia, Finland, France, Greece, Italy, Lithuania, Portugal, Romania, Slovakia, Slovenia and Spain.Furthermore, a drug can now be placed on the Positive Drug List if it is reimbursed by national health insurance funds in at least five of 17 countries. These are Romania, France, Estonia, Greece, Slovakia, Lithuania, Portugal, Spain, Belgium, the Czech Republic, Poland, Latvia, Hungary, Italy, Finland, Denmark and Slovenia.

Croatia compares prices to Slovenia, the Czech Republic and Italy. If not available in any of these, French and Spanish prices are consulted. For both products seeking reimbursement and those reimbursed, prices should not exceed the average price of INN in referenced countries.

Cyprus compares prices in Austria, Greece, France and Sweden. The maximum price should not be larger than the average.

In the Czech Republic, the maximum price of a certain pharmaceutical is set as the average of 3 lowest prices of this pharmaceutical found in the reference basket (reference basket states – All EU countries except for Austria, Bulgaria, Cyprus, Czech Republic, Estonia, Germany, Luxembourg, Malta and Romania).

In Estonia, prices are most commonly compared to Latvia, Lithuania and Hungary, although prices in other EU countries can also be consulted. For reimbursement purposes, the minimum price of the defined daily dose is the benchmark.

Hungary consults prices in all EU and EEA countries. For reimbursement the price has to bethe lowest in the European EconomicArea, and it has to be reimbursed at leastin three countries.Prices of reimbursed products should not be higher than the average of the lowest three in EEA enlarged by 20%.

Kosovo procures medicines through national tenders.

Latvia benchmarks other Baltic states and the EU. The general principle is that prices should not exceed the prices in other Baltic countries and the third lowest price in other EU member states.

Lithuania compares prices to the Czech Republic, Slovakia, Estonia, Poland, Latvia, Hungary, Bulgaria and Romania. The reimbursement level is set as the average price in the reference countries is lowered by 5%.

For medicines seeking reimbursement, FYR Macedonia consults prices in 12 referent countries: Serbia, Croatia, Slovenia, Bulgaria, Greece, Turkey, Poland, Russia, The Netherlands, Germany, France and UK. The reimbursement level is set at the average of the two lowest prices. For reimbursed products, prices are consulted in Serbia, Croatia, Slovenia and Bulgaria.

Malta compares prices of medicines provided in the public sector in Cyprus, Czech Republic, Greece, Spain, Hungary, Italy, Lithuania, Portugal, Sweden, Slovak Republic and the UK. The Maltese price should not be larger than the average price. An algorithm is used for the private sector for price calculation.

Montenegro has in 2011 published a bylaw regulating price comparisons between Slovenia, Serbia and Croatia, but it was never implemented. Medicines are procured through national tenders.

Poland consults prices in all EU 27 countries.

Romania benchmarks prices in Austria, Belgium, Bulgaria, Czech Republic, Greece, Germany, Hungary, Italy, Lithuania, Poland, Slovakia and Spain. The reference price is set at the level of the lowest price in the reference basket.

Serbia consults prices in Croatia, Slovenia and Italy. The price is set at the level of the lowest price from the country basket.

In Slovakia, the price should not exceed the average of the three lowest prices in EU 27.

Slovenia consults prices in France, Germany and Austria. The maximum Slovenian price for originator products is mandated as the lowest of the three. For generics, the average of the average prices in reference countries is multiplied by 68%, and for biosimilars by 72%.

While commonly used for years in all CEE countries but Kosovo and Montenegro as one of the most important price setting criteria, the implementation of international price comparisons in most countries of the region falls short of the clarity and methodological consistency that could be falsely associated with what is in principle a mathematic operation. Variations from calculated prices are abundant. This happens for several reasons. Companies are inclined to push for higher prices than legally mandated as they are aware of the fact that reducing the price in one country starts a domino effect in which a number of other countries will request the same price cut. Regulatory capacity in most CEE countries is weak and government staff can lack resources and knowledge to implement the complex calculations correctly and in regulated time cycles, particularly as the number of referenced countries in a basket tends to increase over time. Price sources are also often problematic. Linguistic issues arise, comparator packs can be confusing, different prices are compared (wholesale, retail, ex factory, etc.) and not all countries publish prices on the internet to the public. Furthermore, for patented products, governments lack negotiating power as if a company declines to accept the calculated price, the only alternative to allowing the concession can be delisting a product and facing patient discontent. Finally, calculation rules change dynamically, either through alterations in reference countries or calculation methodologies which further complicates the procedure.

**Additional pricing mechanisms**

ERP rarely determines the final price of a medicine as a myriad of supplemental pricing and reimbursement rules are currently targeted at specific product groups depending on therapeutic value, patent status and existence of competitor medicines. Cost containment is (although often not explicitly) the common denominator behind most.

ERP, internal pricing comparisons, discounts, pay back agreements, reimbursed prices, copayments and managed entry agreements have become highly multivariate, heavily interlinked between countries and confusingly complex. Price setting regulations are described in countries’ legal frameworks, however the details of the descriptions differ greatly from country to country while the exact timing cycles of price calculations and implementation of methodologies display substantial heterogeneity even within a single country over various years.

In addition, there is a strong link between pricing and reimbursement, as the latter often influences the former, be it through measures such as managed entry agreements, value based pricing, internal price referencing (e.g. therapeutic reference pricing) or through pricing tactics of competitor companies and entry of new molecules to the market.

Hospital tenders are pervasive and used in all CEE countries, although they vary from country to country in the scope of procured products and number of participating hospitals. Serbia and Croatia have recently implemented joint hospital procurement reforms that produced massive savings. For instance, the cost of hospital administered drugs with generic alternatives in Croatia in 2013 decreased by 44,7% while in Serbia in 2012 the cost for all drugs administered in hospitals decreased by 27% after centralized tendering.

Therapeutic value referencing (jumbo clusters) is also common, although again variable in the scope of products for which it is used, the composition of the clusters, the ATC level of clustering (varying from 3 to 5) and the methodologies used to calculate internal reference prices – price per DDD being the most common criterion. It is used in Albania, Bulgaria, Croatia, Czech Republic, Estonia, Hungary, Latvia, FYR Macedonia, Poland, Romania, Serbia and Slovenia.

Managed entry, discount and risk sharing agreements have been used for several years in some form or another in most countries; Bulgaria, Croatia, Estonia, Hungary, Latvia, Lithuania, Poland, Romania, Serbia and Slovenia leading in the implementation and development of these regulatory policies. Other countries are following suit. Little concrete data are publicly known on most financial arrangements as these remain confidential between the administration and companies leading to further perplexities in comparing actual prices paid for medicines between countries.

Hungary, Romania, Latvia and Poland operate market wide claw back agreements that stipulate that any consumption over the budget limit for all pharmaceuticals is to be born in part or in totality by the market authorization holders.

**Generics**

Generic medicines represent around half of the total CEE pharmaceutical market in value terms and almost three quarters in volume terms. Generics have retained a strong market position in the region due to the demand for affordable medicines and the fact that the region is home to a large number of generic companies including Krka, Pliva, Alkaloid, Belupo, Pharma S, BosnaLijek, Gedeon Richter, Polpharma, etc. often enjoying explicit or implicit protection from local governments.

Virtually all countries stimulate prescribing of generic variants compared to branded originators and employ reimbursement rules that stipulate lower prices for generics when seeking reimbursement, albeit to a different degree. Branded generics are a regional specificity, in most countries that have domestic producers not lagging far behind originators in price as originators swiftly adapt prices to retain competitiveness.

Price cuts demanded for reimbursement vary from country to country. For instance, the Croatian Health Insurance fund demands a 30% price decrease from the first generic entry, and an additional 10% for every subsequent etc. Albania, Czech Republic and Bulgaria demand a 20% price cut for the first generic entry, and Romania 35%. The Hungarian Health Insurance Fund is most severe, it demands a 40% price cut from the first generic entry, 20% for the second, 10% for the third and an additional 5% for every subsequent. Estonia requires the first generic to be priced 30% below the originator, the second least 10% cheaper and the next two by an additional 5%.

Prescribing policies vary across the region and are often not strictly enforced. FYR Macedonia, and Lithuania require all medicines to be prescribed by INN. In Poland, Bulgaria, Czech Republic, Slovenia, Croatia, Bosnia and Herzegovina and Serbia the medicines are prescribed by their branded names, although in most of these prescribing by INN is legally allowed. In Hungary, both INN and branded prescriptions are allowed, the former yet not being common practice. In 2012 a pilot project was introduced obliging doctors to prescribe cholesterol lowering drugs solely by INN. From 2012, Latvian authorities require that medicines for newly diagnosed patients are prescribed by INN. In Estonia, Slovakia and Romania, doctors are obliged to prescribe preferably by INN, while branded prescriptions require documenting a reason why they were not prescribed in INN.

Regardless of the prescribing regulation, in most countries an alternative generic may be dispensed with the patient’s consent if cheaper and/or if the prescribed version is not available. This regulation is often abused by wholesalers and manufacturers who stimulate pharmacists to dispense targeted products through higher margin actions.

**Health Technology Assessment**

As is the case in other European countries, CEE countries are increasingly introducing health economic HTA evidence into their reimbursement decision making processes. Poland and Hungary are clearly the front runners in this process, with other countries following suit. The process is still nascent in Albania, Kosovo, Montenegro, Bosnia and Herzegovina, FYR Macedonia, Cyprus and Malta. All countries require a solid overview of studies demonstrating therapeutic value.

Bulgaria, Serbia and Slovakia have partially included HTA in the reimbursement process. Evidence is not obligatory, but may be submitted with reimbursement applications. Croatia requires budget impact analyses but CEA submissions are optional and rarely submitted. While Latvia also does do not formally require CEA, these are commonly submitted. Lithuania formally requires CMA, CEA or CUA while Poland formally requires CEA, CUA or CMA and BIA as do Czech, Hungarian, Slovenian and Estonian authorities. Up until recently, Romanian authorities required CEA and BIA solely for informative purposes, but these have recently become a must.

Most countries such as Estonia, Romania, Slovak Republic, Latvia, Hungary implicitly use WHO’s guidance on 2-3xGDP/capita per QALY as acceptable. In Poland the threshold is set at 105,000 PLN per QALY (3xGDP/capita).

Serbia and Slovakia are considering alternate approaches towards setting the acceptable ICER threshold. Slovak authorities have already in 2011 incorporated into legislation an indicative <35 average salaries limit (excluding orphan products), while the Serbian Health Insurance Fund proposed 3 different thresholds: 3xGDP per capita for most medicines, 6xGDP per capita for medicines that would be used by less than 1000 patients and 9xGDP per capita for oncology treatments.

That said, while most countries have in recent years started introducing health economic arguments into reimbursement deliberations, the overall level of knowledge in health economics in the region (apart from Hungary and Poland) is very low both in the industry and particularly in regulators. Nevertheless, in the future the process will inevitably develop both in skill and in importance.

# Appendix 2 - Glossary

Glossary[[35]](#footnote-36)

Active ingredient:

An Active Pharmaceutical Ingredient (API) is the chemical substance contained in apharmaceutical, which is responsible for its therapeutic effect. Some pharmaceuticals containmore than one active ingredient (combination product).

Brand name:

Name given for marketing purposes to any ready-prepared medicine placed on the marketunder a special name and in a special pack. A brand name may be a protected trademark.

Co-payment:

Insured patient‘s contribution towards the cost of a medical service covered by the insurer. Itcan be expressed as a percentage of the total cost of the service (also known as co-insurance) or as a fixed amount. (WHO)

Counterfeit medicinal product:

The term counterfeit medical product describes a product with a false representation of itsidentity and/or Source. This applies to the product, its container or other packaging or labeling information. Counterfeiting can apply to both branded and generic products.

Cost, Insurance, Freight (CIF):

CIF is a shipping term meaning that the seller must pay the costs, insurance and freight charges necessary to bring the goods to the port of destination.

Dispenser:

A dispenser is a health care professional who is legally qualified to distribute medicines.

Dispensing fee:

Normally a dispensing fee is a fixed fee that pharmacies are allowed to charge per prescribeditem instead of or in addition to a percentage mark-up. The fee more accurately reflects thework involved in dispensing a prescription; a percentage mark-up makes profit dependent onthe sale of expensive medicines.

Distribution:

The division and movement of pharmaceutical products from the premises of the manufacturer of such products, or another central point, to the end user thereof, or to an intermediate point by means of various transport methods, via various storage and/or health establishments.

Formulary:

A formulary is a manual containing clinically oriented summaries of pharmacological information about selected drugs. The manual may also include administrative and regulatory information pertaining to the prescribing and dispensing of drugs).

A national formulary generally concentrates on available and affordable medicines that arerelevant to the treatment of diseases in a particular country. Formularies are also frequentlycreated for different levels of health care, different sectors and for individual hospitals.

Generic:

A pharmaceutical product which has the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal product, and whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies. (WHO)

Generic substitution:

Generic substitution is the practice of substituting a pharmaceutical, whether marketed under a trade name or generic name (branded or unbranded generic), by a pharmaceutical, often acheaper one, containing the same active ingredient(s).

International non-proprietary name:

International Nonproprietary Names (INN) facilitate the identification of pharmaceutical substances or active pharmaceutical ingredients. Each INN is a unique name that is globally recognized and is public property.

International Reference Pricing:

In the WHO/HAI survey measuring prices, availability, affordability and price components ofmedicines, medicine prices are expressed as ratios relative to a standard set of reference pricesto facilitate national and international comparisons. Median prices listed in MSH’s International. Drug Price Indicator Guide have been selected as the most useful standard since they areupdated frequently, are always available and are relatively stable. These prices are recentprocurement prices offered by both not-for-profit and for-profit suppliers to developingcountries for multi-source products.

Manufacturing:

Manufacturing includes all operations of receipt of materials, production, packaging,repackaging, labeling, relabeling, quality control, release, storage and distribution of activepharmaceutical ingredients and related controls.

Marketing authorization:

A legal document issued by the competent drug regulatory authority for the purpose ofmarketing or free distribution of a product after evaluation for safety, efficacy and quality. Itmust set out, inter alia, the name of the product, the pharmaceutical dosage form, thequantitative formula (including excipients) per unit dose (using INNsor national generic names where they exist), the shelf-life and storage conditions, and packaging characteristics. It specifies the information on which authorization is based (e.g. "The product(s) must conform to all the details provided in your application and as modified in subsequent correspondence"). It also contains the product information approved for health professionals and the public, the sales category, the name and address of the holder of the authorization, and the period of validity of the authorization.Once a product has been given marketing authorization, it is included on a list of authorizedproducts – the register – and is often said to be "registered" or to "have registration". Marketauthorization may occasionally also be referred to as a "license" or "product license".

Me too medicine

A me-too medicine is approved after a pioneering product and is defined as comparable or similar but not clinically superior product.

Originator pharmaceutical product:

An originator brand is generally the product that was first authorized world wide for marketing (normally as a patented product) on the basis of the documentation of its efficacy, safety and quality, according to requirements at the time of authorization: e.g. Valium. The originator product always has a brand name; this name may, however, vary across countries.Some substances (e.g. prednisolone, izoniazid) are so old that no originator can be identifiedand the patent was probably never claimed.

Over the counter medicine:

Over-the-counter medicines are medicines that can be sold from licensed dealers withoutprofessional supervision and without prescription. These medicines are suitable for self-medication for minor disease and symptoms.

Parallel import:

Parallel or grey-market imports are not imports of counterfeit products or illegal copies. These are products marketed by the patent owner (or trademark- or copyright-owner, etc) or with the patent owner’s permission in one country and imported into another country without the approval of the patent owner.

Patent:

Patents provide the patent owner with the legal means to prevent others from making, using, or selling the new invention for a limited period of time, subject to a number of exceptions.A patent is not a permit to put a product on the market. A patent only gives an inventor theright to prevent others from using the patented invention. It says nothing about whether theproduct is safe for consumers and whether it can be supplied. Patented pharmaceuticals stillhave to go through rigorous testing and approval before they can be put on the market.

Pharmaceutical product:

A pharmaceutical product is a unique product defined by its active pharmaceutical ingredient,the strength of the active pharmaceutical ingredient, its pharmaceutical form and route ofadministration.

Pharmacovigilance:

Pharmacovigilance is the science and activities relating to the detection, assessment,understanding and prevention of adverse effects or any other drug-related problems.

Reimbursement list:

Reimbursement is the percentage of the reimbursement price (for a service or a medicine)which a third party payer pays. So 100% reimbursement means that the third party payer covers 100% of the reimbursement price / amount of a medicine or service except a possibleprescription fee. A reimbursement list is the list of medicines, which a third party payer pays in part or completely. (WHO)

Reimbursement category:

Medicines eligible for reimbursement are often grouped according to selected characteristics,e.g. route of administration (oral, etc.), main indication (oncology, pediatric, etc.), ATC level,classification (hospital-only, etc.). In many countries different reimbursement rates aredetermined for different reimbursement categories.

Retail distributor:

A retail distributor is a company that sells goods to consumers, e.g. a pharmacy or othermedicines outlet. Many low- and middle- income countries have at least two different types of shops in which medicines can be purchased: pharmacies with a registered pharmacist andmedicines stores, chemists or medicines outlets with paramedical or lay staff.

Retail mark-up:

The retail mark-up is the percentage that retailers (pharmacies) add to cover their costs,including their profit. These costs include those overhead costs that retailers incur in theirpractice, such as rent, staff salaries, repackaging and loss, as well as profit. Retail mark-ups arenot limited to the private sector: the public and other sectors can also use mark-ups to covertheir costs.Mark-ups can vary between products: imported and locally produced medicines often havedifferent mark-ups. Pharmacies may also charge different mark-ups on originator brands andgenerically equivalent products. In some countries, for example, the mark-ups are higher ongeneric equivalents because, even with the markup, they are considered to be affordable.Maximum retail mark-up: In some cases, the government applies a ceiling or maximumpercentage limiting the mark-up that a retailer can add. However, it is also common to find thatthis mark-up is not enforced and much higher percentages can be found in practice.Regressive retail mark-up: In some countries, there may be different maximum mark-ups fordifferent price bands: this is called a ‘regressive mark-up’ and means that the mark-up decreasesas the price of the medicine increases.In countries where prices are not regulated or where regulations are not enforced, there mightbe great variation in retail mark-ups. If medicines are sold in the informal sector (medicineoutlets), price variations can be even greater.

Wholesale:

All activities consisting of procuring, holding, supplying or exporting medicinal products, apart from supplying medicinal products to the public.Such activities are carried out with manufacturers or their depositories, importers, otherwholesale distributors or with pharmacists and persons authorized or entitled to supplymedicinal products to the public in the Member State concerned.Wholesalers have a public service obligation: the obligation to guarantee permanently anadequate range of medicinal products to meet the requirements of a specific geographical areaand to deliver the supplies requested within a very short time over the whole of the area inquestion

Wholesale mark-up:

The wholesale mark-up is the percentage added by the wholesaler or Central Medical Stores to cover overhead costs. These costs encompass overhead expenses such as rent, security,electricity, staff salaries and loss. In some situations, it includes costs to transport medicines to retailers. In the private sector, the markup also includes a profit margin; in the public andmission sector, the margin can provide capital for future investment or cover unforeseenincreases in costs (e.g. inflation or devaluation).If the medicines move through more than one wholesaler on their way to the patient, multiplewholesale mark-ups might be levied. This tends to happen as medicines move from central,urban areas to more rural ones.Maximum wholesale mark-up: In some countries, the government applies a ceiling or maximum percentage limiting the mark-up that a wholesaler can add. In some cases, this mark-up is not enforced and much higher percentages can be observed.Intermediaries that buy drugs from manufacturers, importers or higher-level wholesalers and sell them to lower-level wholesalers, hospitals, or retail pharmacies (AS)

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