

The climate for innovative medicines in the Republic of Macedonia

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Introduction

- ❑ Competition between innovative and generic pharmaceutical companies intensified in last decade
- ❑ Macedonia has limited medicines budget and aims to save on medicines supplies, but also intends to use innovative medicines for first and second-line therapy
- ❑ During financial crisis, health authorities promote use of generics vs. expensive originator medicines

Study objectives

- ❑ Description of circumstances that led to innovative medicines' entry to the market

Study methodology

- ❑ Analysis of national legislation and circumstances that influence innovative medicines' entry to the market

| Legal acts and by-laws | Official Gazette (year) | Characteristics of reimbursement policies and medicines prices |
|--|-------------------------|---|
| Law for supplementing and amending the Law on medicinal products and medical devices | 88/2010 | New paragraph allows by-laws to treat price formation at technical details level |
| Methodology for medicines' single price structure | 156/11 45/12 | <p><u>Referent pricing:</u> Slovenia, Bulgaria, Netherlands, Poland, UK, France, Croatia, Serbia, Greece, Germany, Turkey and Russia</p> <p><u>Maximum wholesale medicines price:</u> average value of 2 lowest comparison wholesale prices from referent countries</p> <p><u>Fees within wholesale medicine price:</u> wholesale fees, custom fees, other import fees</p> <p><u>Retail margin:</u> as % of wholesale prices (28, 25, 20% up to 1,200 MKD).</p> <p><u>Medicine pricing structure:</u> suggested retail price – same or lower price calculated by this methodology</p> <p><u>Increase of medicines prices</u> - pharmacoeconomic study and/or calculations for justification</p> <p><u>Brand medicines or innovative medicines</u></p> <p>Maximum price – average value of 2 lowest wholesale prices of brand medicine from same manufacturer in referent countries</p> <p><u>Pharmacoeconomics indicators</u></p> |

| Legal acts and by-laws | Official Gazette | Characteristics of reimbursement policies and medicines prices |
|--|----------------------|--|
| Law for supplementing and amending the Law on medicinal products and medical devices | 11/2012 | Option given for parallel importation of medicines |
| Law for supplementing and amending the Health Insurance Law | 26/2012 | <p>Modification of mode and methodology to establish the Health Insurance Fund (HIF) medicines reimbursement list (Positive list): Ordinance passed by Government</p> <p>14 expert committees established by Government according to ATC, made from 17 members (14 MDs, 1 MOH representative, 1 clinical pharmacologist/pharmacist) 1year mandate.</p> <p>Committees make decisions based on prior opinion given by appropriate university clinic.</p> |
| Health Insurance Fund (HIF) medicines reimbursement list (Positive list) | 81/2012 revised text | <p>Number of amendments and additions</p> <ul style="list-style-type: none"> • medicines dispensed according to INN and ATC classification • preferences towards generic medicines • small number of innovative medicines • Listed indications for reimbursement • 377 medicines on primary care / 343 medicines on hospital positive list (by generic name) |

| Legal acts and by-laws | Official Gazette | Characteristics of reimbursement policies and medicines prices |
|---|------------------|--|
| Ordinance on mode and methodology for HIF medicines reimbursement list | 116/2012 | <p>Medicines on the list</p> <ul style="list-style-type: none"> • List A – medicines from PHC, dispensed at HIF-contracted pharmacies • List B - medicines from hospital healthcare • Medicines grouped according to ATC, INN, prescribing regime, indications, application site, dispensing of special group medicines, dispensing and use of medicines according to indications or remarks • Application procedure for adding/removing medicines on list • Harmonisation with HIF financial possibilities • Incorporation of scientific evidence on drug efficacy, pharmacotherapeutic/pharmaco-economic indicators and medicines price • Incorporation of pharmaco-economic and financial analysis, wholesale prices according to DDD and info on medicines inclusion on positive lists in EU countries/other with comparative economic systems <p>List revision at least annually</p> |
| Rulebook on the criteria and procedures to establish medicines reference prices | 158/09 138/10 | <ul style="list-style-type: none"> • Referent countries: Slovenia, Croatia, Bulgaria, Serbia • Harmonisation of reference price with PPP coefficient • Price of medicine with no generic competitor - max 10%, and with generic competitor - max 79,23% of average comparison price • Option for therapeutic equivalent with same efficiency/safety • Reference prices established on 10 January each year. |

Discussion

- ❑ By-laws explain medicines pricing and registration procedure (incl. 5% VAT)
- ❑ Reference pricing methodology sets low unique medicines prices

- ❑ Only medicines of special interest can be up to 20% higher than average wholesale prices in referent countries
- ❑ The complexity of positive list' procedure delays and hampers the inclusion of new medicines on the list
- ❑ HIF establishes referent prices, and negotiates with companies the price alignment of brand medicines and predetermined reference prices of generic medicines to achieve lower prices
- ❑ National medicines budget reached 154 million Euros
- ❑ 3510 registered medicines: 2623 generic (75%) and 152 innovative (4%)

| Requests for inclusion of innovative medicines on the reimbursement list (2007 – 2012) | | | | |
|--|-------------------|----------------------|-----------------------------------|-------------------|
| ATC code | INN | Name of the medicine | Manufacturer | Registration date |
| L01XA03 | oxaliplatin | Eloxatin | Aventis farma Sanofi-Aventis | 13.05.2010 |
| | | Oksaliplatin | Cipla Ltd. | 30.06.2009 |
| | | | EBEWE Pharma | 29.03.2012 |
| | | | PLIVA LACHEMA as | 30.06.2009 |
| L01XC07 | bevacizumab | Avastin | Hoffman la Roche | 28.09.2010 |
| L01XE01 | imatinib * | Glivec | NOVARTIS Pharma | 25.03.2011 |
| | | Anzovip | ZDRAVLJE A.D. - Leskovac | 25.12.2012 |
| | | Imakrebin | REMEDICA Ltd – Limasol, Cyprus | 24.01.2013 |
| | | Plivatinib | PLIVA Hrvatska | 29.11.2012 |
| L01XE03 | erlotinib | Tarceva | Hoffman la Roche | 28.10.2010 |
| L01XC04 | alemtuzimab | Mabcampath | Boehringer ingelheim | 28.10.2010 |
| B01AX06 | rivaroxaban | Xarleto | BAYER SCHERING PHARMA AG | 30.12.2008 |

Conclusion and recommendations (1)

- ❑ Republic of Macedonia has limited drug budget and aims to save the resources for drug supplies.
- ❑ It also aims to allow market entrance of innovative medicines, especially for first- and second-line treatments in line with its financial possibilities.
- ❑ Regulation has been recently modified to facilitate market entrance for innovative medicines. But, frequent modifications and adjustments delayed the process of their efficient implementation
- ❑ Generic prescribing and reference pricing have a negative impact on brand medicines and limit choices of prescribers and patients, but save budget resources that can be used to include innovative medicines on the market and the reimbursement list.
- ❑ Parallel importation is beneficial to market offer, competition and medicines prices, but hampers the financial sustainability of the innovative companies' representative offices.

Conclusion and recommendations (2)

- ❑ Discontinued legal procedures and complicated procedures delay its completion and inclusion of innovative medicines on the positive list
- ❑ Reduction of medicines prices with unique prices / reference prices methodologies for reimbursed medicines can free resources for new medicines, but lower prices decrease innovative companies' interest to enter the market
- ❑ Savings can be made by (1) rationale positive list, (2) rational use of medicines in hospital and (3) introduction of pharmacoeconomic aspects in practice, which can be used to include new medicines for patient care.
- ❑ Inclusion of expensive innovative medicines shall be based on scientific evidence on drug efficiency (first- and second-line therapies), pharmacotherapeutic and pharmaco-economic indicators and HIF financial possibilities.
- ❑ Presence of innovative medicines on Macedonian market and inclusion on positive list shall be done in line with experience of EU and neighboring countries with comparative economic systems