Market entry of 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	Referent pricing: Slovenia, Bulgaria, Netherlands, Poland, UK, France, Croatia, Serbia, Greece, Germany, Turkey and Russia Maximum wholesale medicines price: average value of 2 lowest comparison wholesale prices from referent countries Fees within wholesale medicine price: wholesale fees, custom fees, other import fees Retail margin: as % of wholesale prices (28, 25, 20% up to 1,200 MKD). Medicine pricing structure: suggested retail price – same or lower price calculated by this methodology Increase of medicines prices - pharmacoeconomic study and/or calculations for justification Brand medicines or innovative medicines Maximum price – average value of 2 lowest wholesale prices of brand medicine from same manufacturer in referent countries Pharmacoeconomics indicators

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	Modification of mode and methodology to establish the Health Insurance Fund (HIF) medicines reimbursement list (Positive list): Ordinance passed by Government 14 expert committees established by Government according to ATC, made from 17 members (14 MDs, 1 MOH representative, 1 clinical pharmacologist/pharmacist) 1year mandate. Committees make decisions based on prior opinion given by appropriate university clinic.
Health Insurance Fund (HIF) medicines reimbursement list (Positive list)	81/2012 revised text	Number of amendments and additions • 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	Medicines on the list •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, pharmaco-therapeutic/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 List revision at least annually
Rulebook on the criteria and procedures to establish medicines reference prices	158/09 138/10	• 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 Oksaliplatin	Aventis farma Sanofi-Aventis Cipla Ltd. EBEWE Pharma PLIVA LACHEMA as	13.05.2010 30.06.2009 29.03.2012 30.06.2009
L01XC07	bevacizumab	Avastin	Hoffman la Roche	28.09.2010
L01XE01	**imatinib ***	Glivec Anzovip Imakrebin Plivatinib	NOVARTIS Pharma ZDRAVLJE A.D. - Leskovac REMEDICA Ltd – Limasol, Cyprus PLIVA Hrvatska	25.03.2011 25.12.2012 24.01.2013 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), pharmaco-therapeutic 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