

## Improving the managed introduction of new medicines; sharing experiences to aid authorities across Europe

The Managed Introduction of New Medicines, Warsaw, Poland 11 to 13 May, 2015

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(Accepted for publication Expert Review Pharmacoeconomics and Outcomes Research – Please keep CONFIDENTIAL).

### Abstract

The 3-day course on the managed introduction of new drugs was organised by the Piperska group together with the Agency for Health Technology Assessment and Tariff System (AOTMiT) and WHO Europe to share experiences and case histories among health authority and health insurance company personnel, academics and those from commercial organisations from across Europe on potential ways to optimise the managed entry of new medicines. This starts pre-launch with horizon scanning and budgeting, then peri-launch including critical drug evaluation, and finally post launch including monitoring prescribing of new medicines against agreed guidance and indicators. There were also discussions on issues regarding managed entry schemes and procurement strategies including biosimilars.

Key words: Biosimilars, DTCs, horizon scanning, HTA, indicators, managed entry schemes, medicines.

### Introduction

Pharmaceutical expenditure is a concern driven by factors including new high priced medicines (1-4), resulting in new models, starting pre-launch, through peri-launch to post launch (1, 2). These three pillars formed the basis of the 3-day course organised by the Piperska group (5), the Agency for Health Technology Assessment and Tariff System (AOTMiT) (6) and WHO Europe.

## Course proceedings (key highlights)

Beata Małecka-Libera, the Secretary of State in the Polish Ministry of Health, discussed the need for data on efficacy and cost effectiveness and the role of AOTMiT when assessing the value of new medicines. As a Government Plenipotentiary for the draft Act on public health, she emphasised that access to new medicines is important but underlined that there are numerous non-drug interventions carried out by authorities that can improve the health of the population.

Hanne Bak-Pedersen discussed the principles for the appropriate use of medicines and current challenges with over 16,000 medicines in development (7), as well as the importance of making transparent, evidence informed choices when expanding benefit packages. Access to essential, quality and affordable medicines is central to achieving universal health coverage. Proposals include developing new models (4) and using HTA to support reimbursement negotiations as well as formulating demand-side strategies.

Poland is also developing strategies to enhance the rational use of medicines, outlined by the president of the National Health Fund - Tadeusz Jędrzejczyk. The introduction of limit groups and limits that promote cheaper generics help control expenditures, with pharmacies obligated to inform customers about cheaper generics. Pharmaceutical manufacturers also partly cover over-budget expenditure through pay-back systems. Monitoring prescribing and influencing prescribers reduces inappropriate medicine use and costs, including measures to limit physicians' writing that medicines cannot be substituted. Future measures include additional education of physicians and patients about medicines and potential alternatives.

Rickard Malmstrom discussed the experiences in the Stockholm Region based on the 'Wise List', encompassing approximately 200 medicines (8). High adherence is achieved by involving 20 expert groups, comprehensive communication programmes and regular feedback (9). A step wise model for new medicines has been in operation since 2006 (10). Critical drug evaluation reports for new medicines are available up to six months before launch, with joint guidelines produced before launch. The comprehensive pre-launch campaign with dabigatran limited bleeding episodes in practice (11), and agreed guidance limited ipilimumab for malignant melanoma given potential costs of approximately 40million SEK (Euro 4.3 million).

Horizon scanning is operated by 4-county collaboration in Sweden, including identification and filtering, prioritization, early assessment, dissemination and monitoring. The annual forecasting report in Stockholm is published by March each year (10). Roberta Joppi discussed the activities of EuroScan as well as the Italian Horizon Scanning project (12). The latter has four specific aims: (i) producing periodical lists of emerging medicines for which marketing authorization is expected within 12-36 months; (ii) evaluating clinical impact and cost effectiveness/ budget impact of new medicines; (iii) giving well-timed information to authorities and (iv) identifying further research fields.

Richard Torbett (EFPIA) stressed investment is needed for new medicines to support ageing populations (3,7). This provides a solid framework for 'value' discussions, entailing a four stage process including agreeing outcome metrics as well as measuring and making the results transparent. As a result, aligning 'traditional' and 'Big Data' approaches to support outcomes focused patient care.

Małgorzata Bała discussed key aspects regarding critical evaluation of new medicines including (i) systematic error; (ii) systematic disposition of trial designs to produce results consistently better or worse than others; (iii) tendency to deviate in one direction from a true value; (iv) threats to internal validity of studies. Biases include (i) selection bias, (ii) performance bias, (iii) detection bias; (iv) attrition bias and (v) reporting bias (13).

Anna Zawada discussed critical evaluation of new medicines by AOTMiT. The current threshold for economic effectiveness (ICER) is  $\leq 3 \times \text{GDP}$  per capita (currently PLN 119,600; €29,200) for all medicines including orphan medicines, helped by narrow indications and risk sharing schemes. In 2015, there were 20 submissions. Added clinical value was proved in only 6 cases. In 6 cases, the budget impact estimation was criticized - in 2 cases estimations were much higher than in the submission and in 2 cases Agency estimations were lower.

Key reimbursement criteria for new medicines in Slovenia include: (i) public health priority; (ii) clinical criteria; (iii) economic criteria including an economic analysis (ICER current 1.5 x GDP at 25 000 €/QALY) and budget impact analysis (first three years); (iv) ethical criteria, e.g. orphan diseases and (v) reference sources. Discounts, rebates, price – volume agreements/ pay-back schemes or performance-based agreements are taken into consideration. The latter only for the most expensive medicines.

Reimbursement criteria for new medicines in Lithuania include: (i) therapeutic value including level of innovation – 2 to 5 points (5 for a new active substance where no previous treatment) and therapeutic benefit - 3 to 10 points with 10 points for a new medicine with considerable value, and with 1 point deducted for concerns with efficacy, safety or QoL, (ii) economic value - based on pharmacoeconomic value (score 1.5, 3, 4.5) and price (0, 1, 2 or 3 where 3 is the lowest price in Europe based on 15 countries) and (iii) budget impact. For positive listing, new medicines must have (i) therapeutic value >9; (ii) pharmacoeconomic value >4 and (iii) negative (neutral) impact on NHIF budget. If therapeutic value >11; pharmacoeconomic value >4, and positive impact to NHIF budget, subsequently placed on a waiting list. In 2014, 59 decisions of which 22 were positive, 24 negative and 13 medicines placed on the waiting list. The waiting list is revised every 6 month, and if budget permits medicines from the waiting list are included in the positive list.

The Scottish Medicines Consortium (SMC) deals with uncertainty by (i) Pre-submission Guidance to Manufacturers stressing the need to test uncertainty; (ii) validation of assumptions and requests for additional analysis during NDC review; (iii) discussions regarding orphan medicines and other modifiers during SMC discussions. Patient access schemes (PAS) can enhance the value of new medicines, with these issues encompassed in SMC's guidance to manufacturers (14). Angela Timoney also discussed formularies in Scotland including the Lothian Region to improve medicine use, based on their 2013 to 2016 Pharmacy Strategy (15) and their Strategic Workplan. NHS Lothian has a strong record of governance in medicines management including the Lothian Joint Formulary giving first and second line choices. Key elements to enhance formulary use include making them easy to follow and clinically attractive, being flexible and responsive with regular updates, and thinking locally whilst acting nationally

Germany also formally assess the level of innovation of new medicines based on a six-point scale and linked to prices (16). 132 substances have been assessed (as of early March 2015). Of these, 37 had additional benefit; 26 with partial additional benefit; 55 without additional benefit; 6 exempt and 8 cancelled/ withdrawn. Factors influencing contracted prices include innovation levels and prices after deducting discounts among 15 European countries, purchasing power adjusted. Estimated savings of €630 million were generated from these negotiations between 2012 and 2014.

Bjorn Wettermark discussed monitoring the utilization and outcome of new medicines and experience of registries (17). Key elements include relevant and valid data on exposure and outcomes, classification systems, quality indicators, robust and valid methods. Study designs can be descriptive, analytical or interventional.

Key messages for developing quality indicators (QIs), building on suggestions for new medicines (18), include: (i) using only valid and reliable indicators to assess quality use of medicines; (ii) QIs are not a magic bullet but are important tools; (iii) Prescribing QIs should be developed using systematic methods; (iv) QIs must take implementation issues into account. Dimensions include (i) perspective; (ii) structure - process – outcome; (iii) Drug, disease or patient-oriented indicators. Indicators in Germany to improve prescribing include monitoring drug costs among physicians, their share of generic scripts and share of 'me-to scripts' especially with high potential savings. QIs include share of prescriptions causing adverse reactions and share of elderly patients receiving potentially inadequate medication, especially as 44 % of the elderly are exposed to at least one potential interaction of at least moderate degree and 14 % to a severe degree. There is now a 2015 framework for economic prescribing including enalapril, lisinopril, and ramipril as 75% of DDDs of all renin-angiotensin inhibitors including aliskeren.

Successful multifaceted approaches in Slovenia to reduce antibiotic utilisation involved extensive educational programmes, QIs and prescribing restrictions (19). There are also ongoing programmes to reduce polypharmacy (16) involving QIs and Pharmacotherapy groups. Measures in Poland to

reduce antibiotic utilisation include making prescriptions valid for 7 days, specifying the antibiotic spectrum and ideally using sensitivity analysis. However this is not necessary if physicians are cognisant of the likely causes of the infection. This initiative reduced antibiotic prescribing and costs, e.g. 23, 941 million packages in 2013 down from 31,549 in 2011 and reimbursed costs down from PLN 361, 849 million in 2011 to PLN 275,121 million in 2013.

The WHO recently updated its Essential Medicines List including oncology medicines (20). Key issues included defining clinically relevant benefits alongside the high cost of new cancer medicines (1,4,21).

Finally, the goal of the Norwegian Drug procurement cooperation (LIS) is to achieve good prices for pharmaceuticals and reduce costs. In 2015, Orion offered a 69% discount for biosimilar infliximab compared with the originator tender price (REMICADE) and 72% compared with its list price (18). Concerns with potential side-effects are being countered by the Ministry of Health funding NOR-SWITCH to comparing originators and biosimilars (22). Other successes included paclitaxel at 149N Kroner for 50mls in 2012 vs. 13, 474 for the originator in 2000.

The course was well received (maximum score of 5) with speakers knowledgeable in their area and clarifying the content (4.8 to 4.9), the content appropriate for the audience with appropriate teaching methods (4.5 to 4.8), which could be applied in practice to achieve personal aims (4.6), and enhance people's expertise somewhat (44%) and substantially (56%). Everyone recommended the course to others.

### **Financial disclosures and competing interests**

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript.

No writing assistance was utilized in the production of this manuscript.

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