

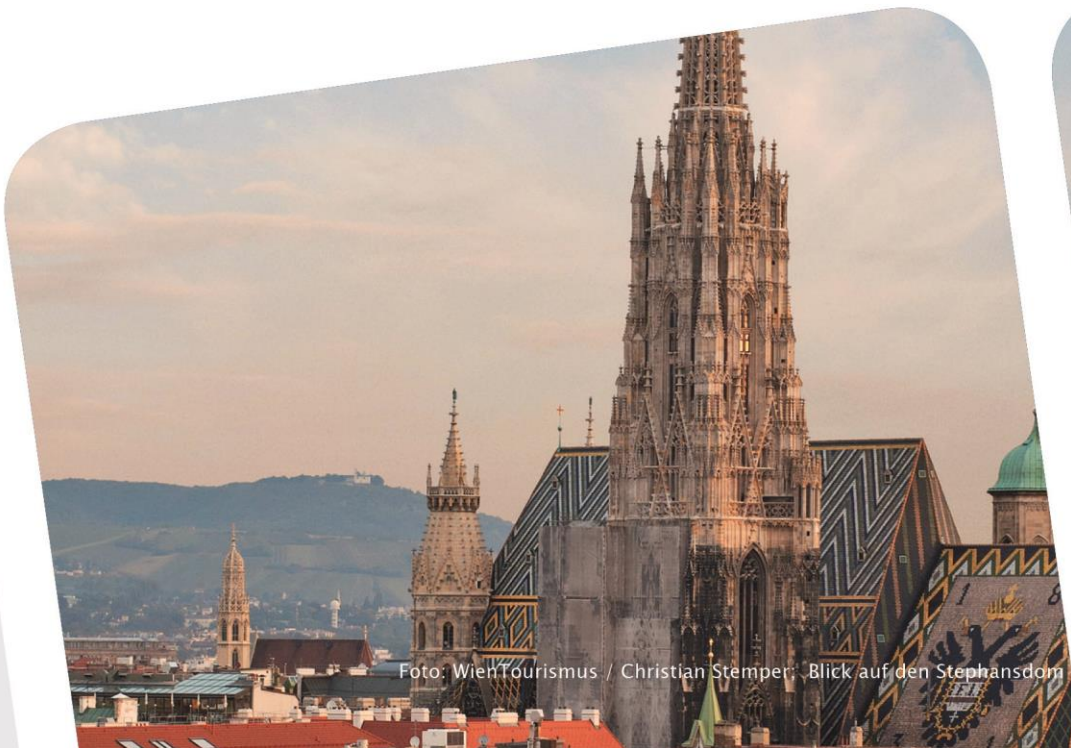
# 4th PPRI Conference Medicines access challenge - The value of pricing and reimbursement policies

Wednesday, 23 October 2019 -  
Thursday, 24 October 2019

Vienna, Austria



## ABSTRACT POSTER BOOK



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affiliated to the Pharmacoeconomics Department at the  
Austrian National Public Health Institute (Gesundheit Österreich GmbH) in Vienna  
Contact: [ppri@goeg.at](mailto:ppri@goeg.at)

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download after the conference at the conference website.



# One third of the total budget went for Antibiotics while hey are cheap

## Analysing and controlling of Pharmaceutical Expenditures of National Health Insurance Fund, Sudan: Paying for value

 Isam Eldin Ahmed  
National Health Insurance Fund, Khartoum,Sudan

### Background

Inaccessibility to medicines is a common problem worldwide

The Pharmaceutical Expenditures represent 45% out of the total health expenditures of the National Health Insurance Fund (NHIF).

In November 2016 the Central Bank of Sudan has Liberalized the exchange rate.

### Objective

to analyze the total cost of pharmaceuticals of NHIF in Sudan to find opportunity for cost reduction

### METHODS

A total cost analysis was performed using ABC, VEN and Therapeutic Categories tools.

The Pharmaceuticals purchased by the NHIF, Sudan in 2016 were analysed. Outcome measure(s): the percentage of the cost of the ten costly medicines, the cost of the top 20% of the items.

### Conclusions and lessons learned:

The main strategies to reduce the cost and improve the use of medicines would be implementation of antimicrobial policy and focus on local manufacturers.

### Results

Table 1: The ten high-cost medicines in 2016

NO	Item Description	UOM	Unit price in SDG	Quantity	Total medicines cost	% of total medicines cost
1	Clopidogril 75mg tab	Tab	6.995	2,163,000.00	15,130,185.00	4.54
2	Insulin mixed	Vial	33.333	357,600.00	11,919,988.08	3.57
3	Artemether 80mg/ml injection	Amp	2.5	4,080,400.00	10,201,000.00	3.06
4	Cefiximetrihydrate 400mg capsule	Caps	3.45	2,521,880.00	8,700,486.00	2.61
5	Amoxicillin 500mg +clavulanic acid125mg. 625mg tab	Tab	1.38	5,202,104.00	7,178,903.52	2.15
6	Ceftriaxone sodium 1gm injection	Vial	8.5	718,700.00	6,108,950.00	1.83
7	Recombinant Human Erythropoietin 4000 IU/1ml for I.V, S.C	Amp	40	148,870.00	5,954,800.00	1.79
8	Amoxicillin400+ Clavulonic acid 57mg suspension (70ml/Bottle)	Bott	24	243,900.00	5,853,600.00	1.75
9	Diclofenac 75 mg inj	Amp	5	1,013,200.00	5,066,000.00	1.52
10	Artemether 40mg/ml injection	Amp	2	2,433,600.00	4,867,200.00	1.46
TOTAL					80,981,112.60	24.28

Figure 1: ABC analysis of usage of medicines in NHIF

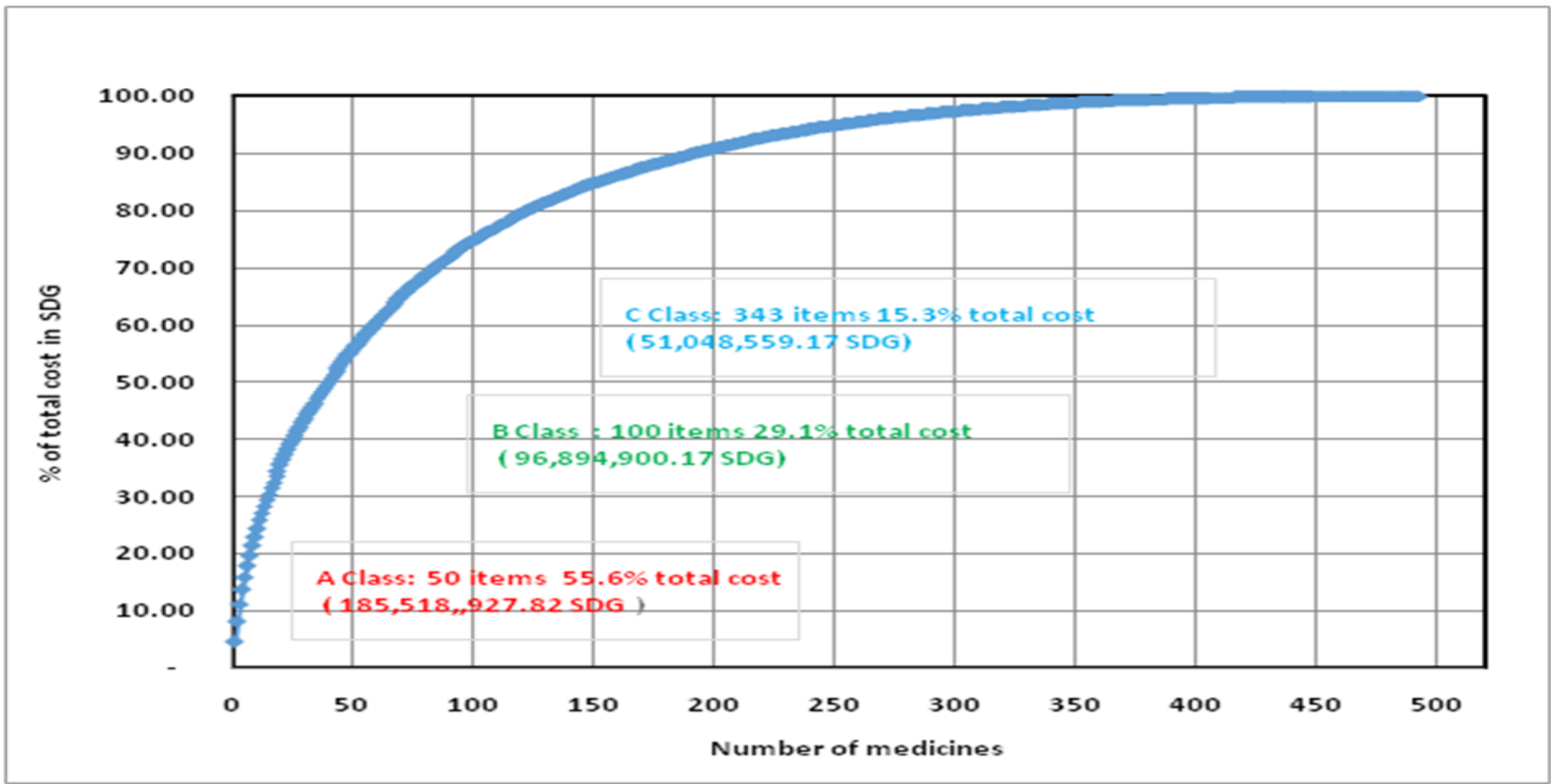
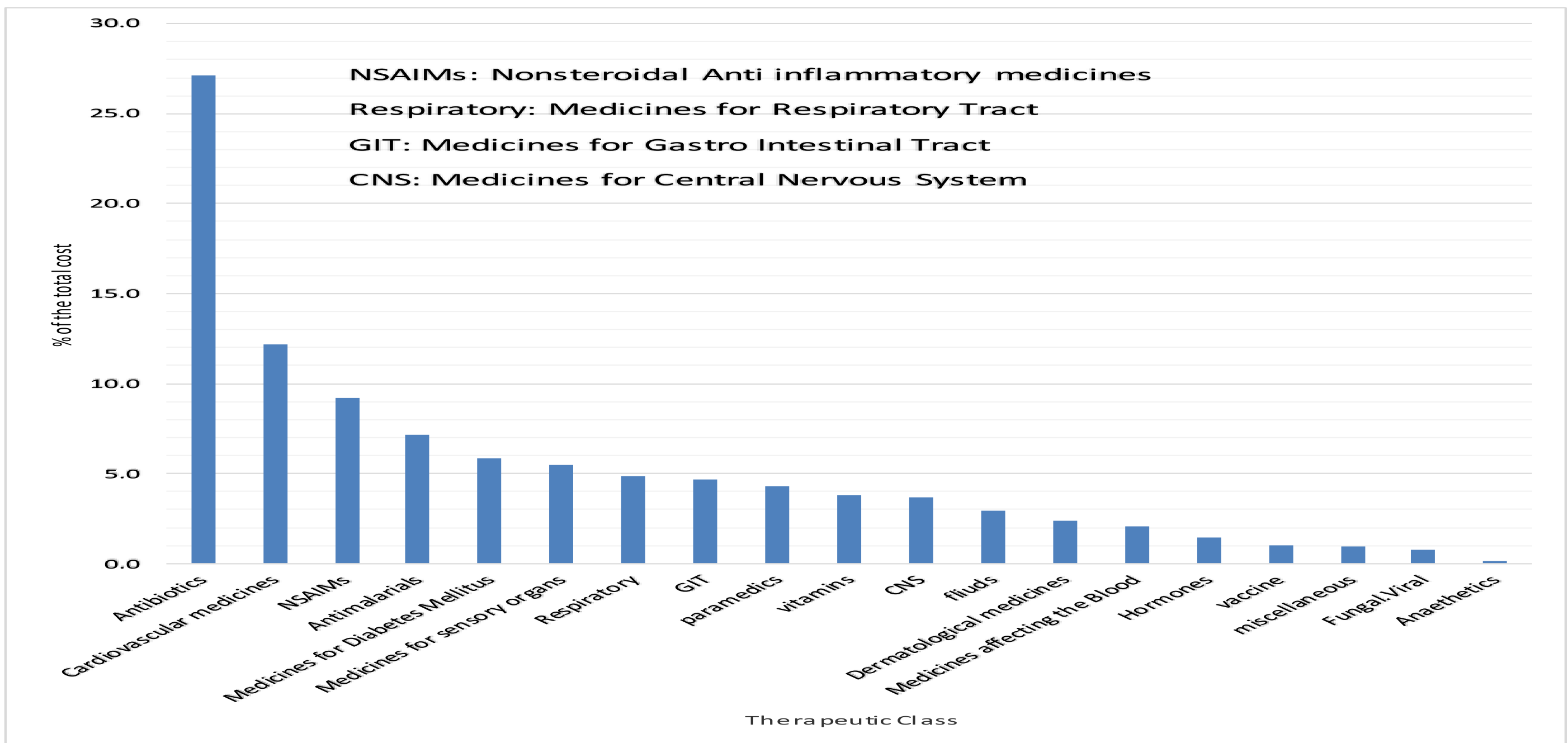


Figure 2: The cost of medicines by therapeutics class





# BIOSIMILAR UPTAKE IN DENMARK – A REVIEW OF SUCCESS

Successful implementation in Denmark is shown very clearly in these two cases of Infliximab 2015 and Etanercept 2016 (Figure 1A & 1B)

## BACKGROUND AND OBJECTIVE

Biosimilar uptake in Denmark has evolved significantly over the last decade. As a procurement body, Amgros has documented its learnings over time. The process has been evaluated and there has been focus on how to ensure successful biosimilar uptake, with each step in the process being considered equally important. The learning curve

for the local Danish biosimilar task force has been steep, and the task force has made recommendations on where to focus in the process of introducing biosimilars. The purpose is to describe the evolution and share recommendations based on the success of biosimilar uptake in Denmark.

## METHODOLOGY

The abstract is based on a single case study using quantitative register data as well as qualitative data from evaluations in each phase of the process. The abstract focuses on one single therapeutic area with implementation of three

biosimilars by looking at market shares on treatment days in different countries for: Infliximab and Etanercept, Figure 1A & 1B, and Adalimumab, Figure 2.

## HOW IT WAS DONE

The biosimilar implementation process (just below) in Denmark is led by a Biosimilar task force. Key learnings are that the partnerships (Figure 3) improve each step in the planning and execution

phase throughout the whole process and make a successful set-up for implementation and uptake of biosimilars.

Planning / exploring of obstacles

Involvement and dialogue

Execution, implementation and follow-up

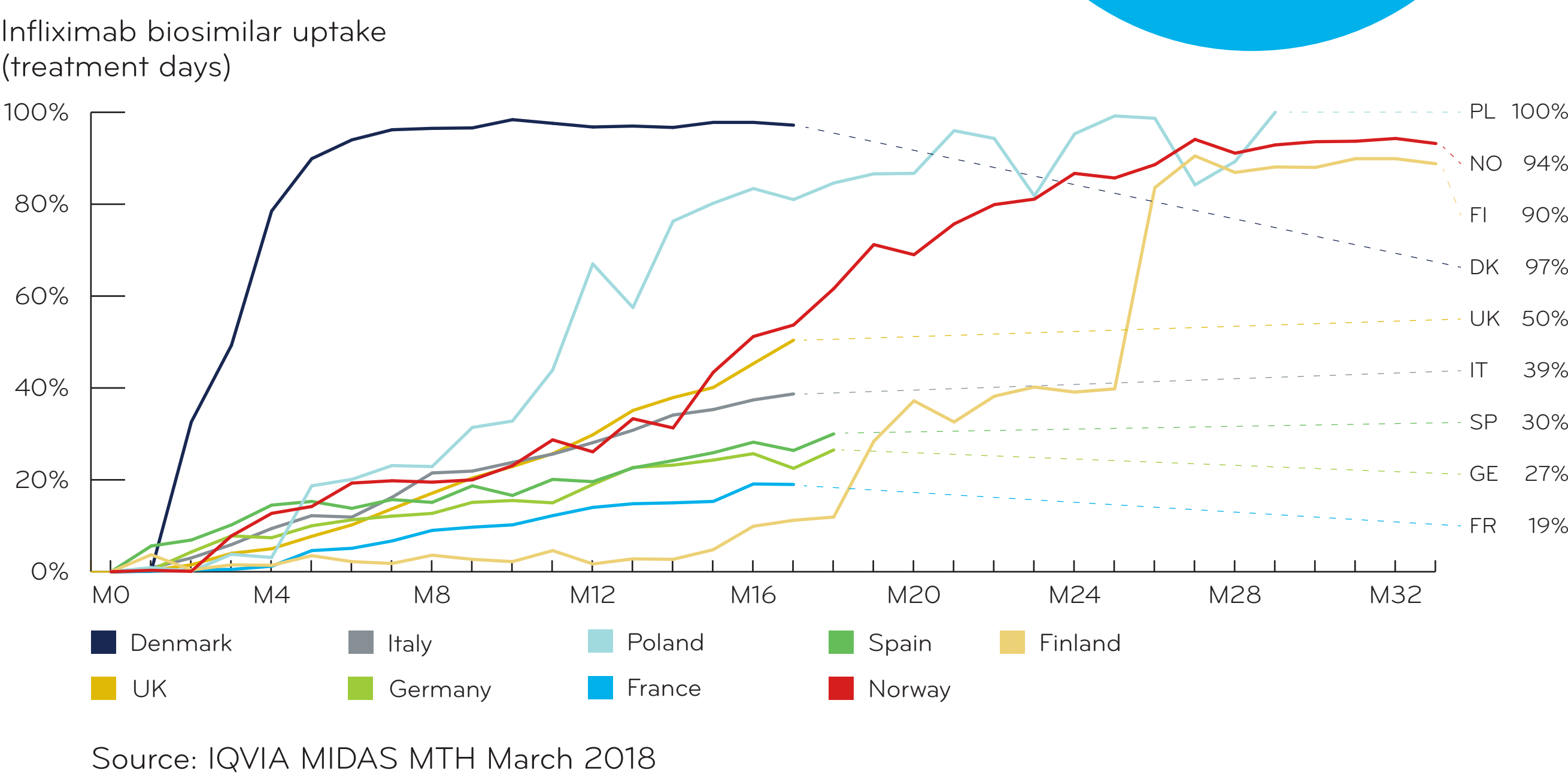
<b>Co-planning with clinical user and supplier</b> <ul style="list-style-type: none"><li>Timing is key!</li><li><b>Clinical users</b> (nurses, doctors, drug committees and pharmacists)<ul style="list-style-type: none"><li>Types of obstacles in relation to switching to a biosimilar at the clinic?</li><li>Change is always a challenge</li><li>New clinical set-up and need for additional personnel?</li><li>IT system</li></ul></li><li><b>Supplier</b><ul style="list-style-type: none"><li>Possibilities for introduction of a biosimilar in Denmark</li><li>Supply issues and 100% delivery</li><li>Timing for launch</li></ul></li></ul>	<b>Involvement of specialists (including the Danish Medicines Council)</b> <ul style="list-style-type: none"><li>Guidelines within therapeutic areas</li><li>Statement from specialists "on the use of biosimilar in the specific patient group"</li></ul> <b>Involvement in the implementation set-up in the regions</b> <ul style="list-style-type: none"><li>Doctors, nurses, drug committees and pharmacists</li></ul> <b>Involvement of the patient organisation – patient information material</b> <ul style="list-style-type: none"><li>Danish Medicines Agency and patient organisations – biosimilars in general</li><li>Biosimilar task force and patient organisations – product specific</li></ul>	<b>Execution</b> <ul style="list-style-type: none"><li>Tender period and new tender prices</li><li>Execution of the "specific scenario"</li><li>Dependent on prices, timing of supply issues</li></ul> <b>Follow-up</b> <ul style="list-style-type: none"><li>Practical support during launch and follow-up on sales</li><li>Patient databases to follow up</li><li>Drug committees and implementation issues</li><li>Learning and evaluation =&gt; key to next launch</li></ul>
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## CONCLUSIONS AND LESSONS LEARNED

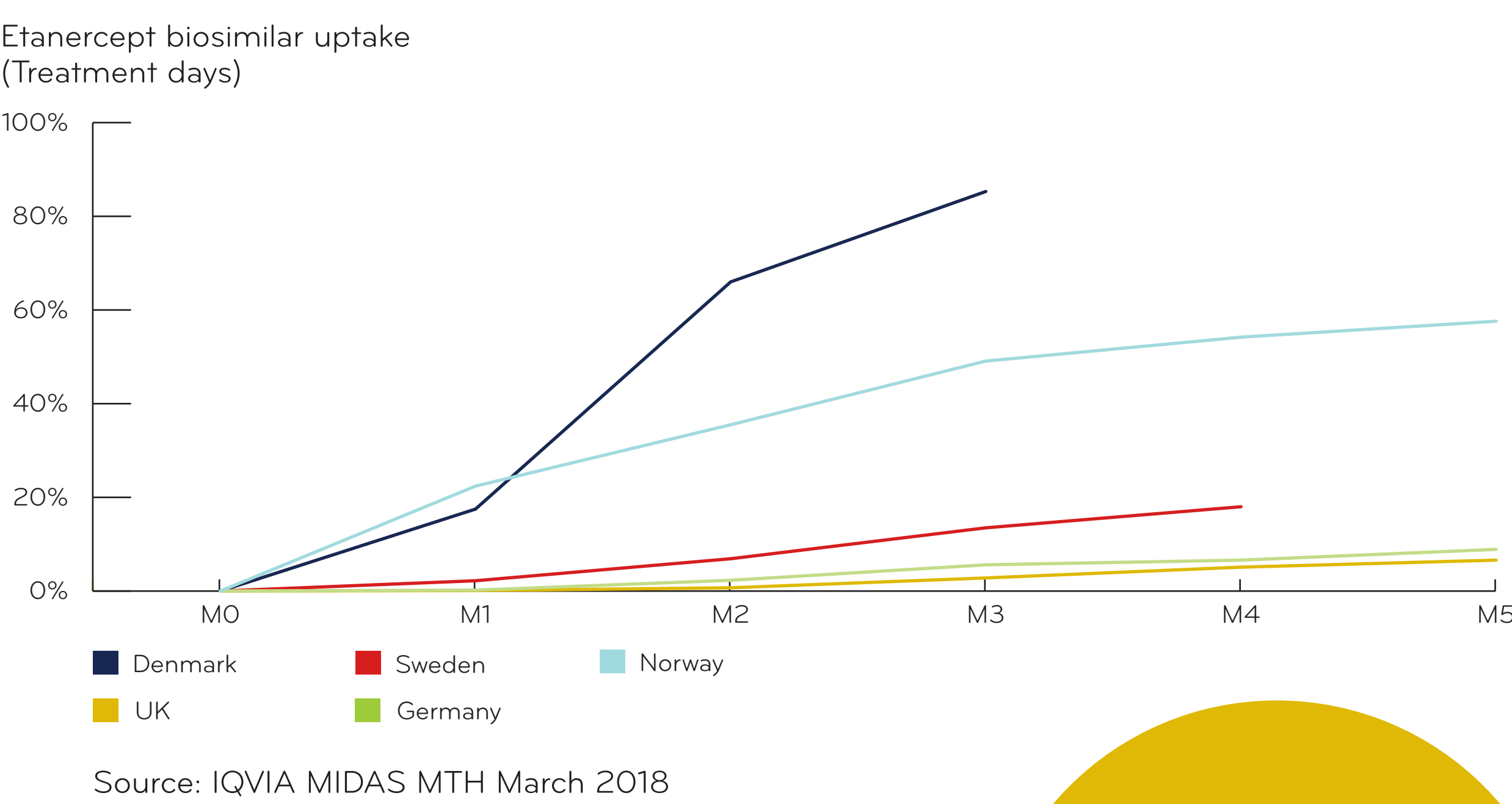
As a procurement body, Amgros developed a set-up where Planning, Dialogue and Involvement (Figure 3) are important to reach the target: successful implementation of a biosimilar in Denmark.

The learnings have involved several elements, both organisational structure and insight sharing as well as on the practical and logistical side after the procurement has been finalized.

FIGUR 1A INFLIXIMAB BIOSIMILAR MARKET SHARE

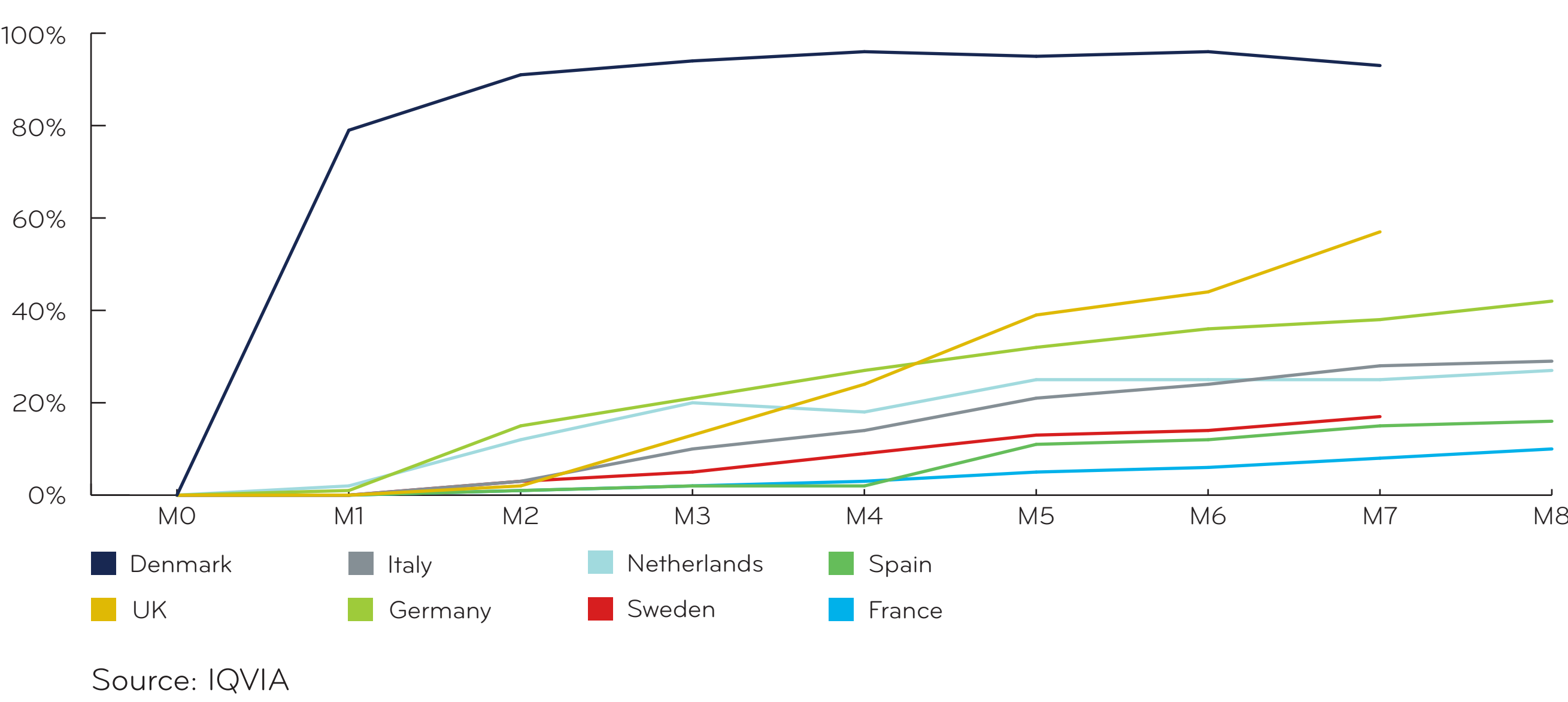


FIGUR 1B ETANERCEPT BIOSIMILAR MARKET SHARE

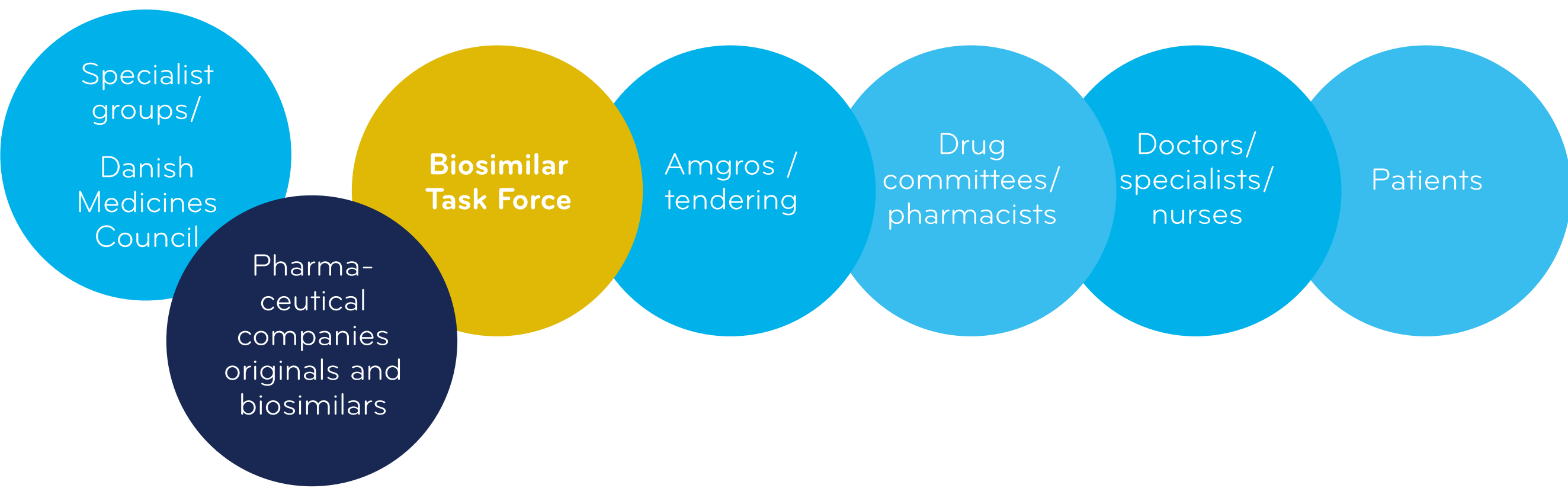


With quick implementation of the Adalimumab biosimilar, Denmark saved EUR 1 mill. per week in the first year

FIGUR 2 IMPLEMENTATION OF BIOSIMILAR ADALIMUMAB (2018) ON TREATMENT DAYS IN DIFFERENT COUNTRIES



FIGUR 3 PARTNERSHIP: PLANNING, DIALOGUE, INVOLVEMENT FLOW





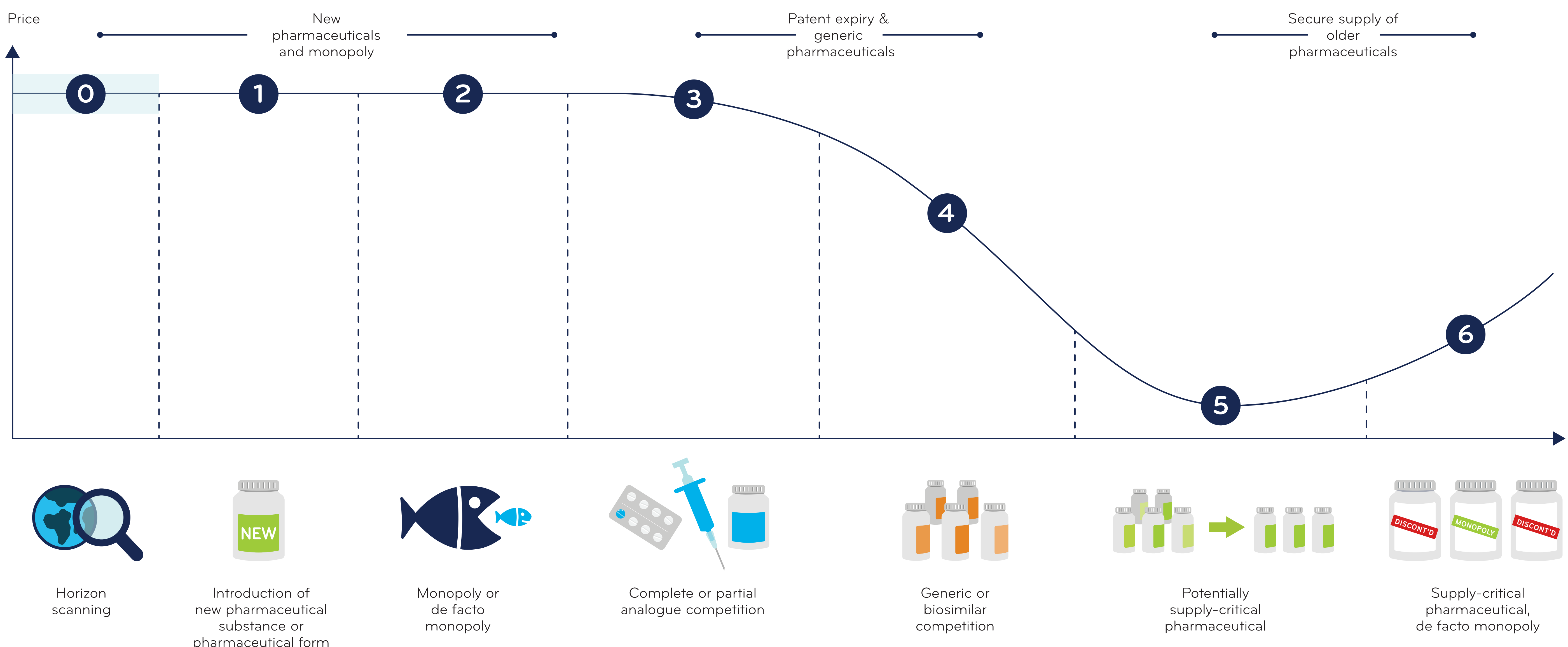
# JOINT PROCUREMENT

## – LEARNINGS FROM A PILOT ON JOINT PROCUREMENT OF OLDER PRODUCTS

Joint procurement pilot with partner countries in the Nordic countries resulted in efficient competition for older pharmaceuticals, with potential future benefits for constrained supply

THE CHALLENGES ARE THE SAME THROUGHOUT THE WORLD

FIGUR 1 PRODUCT LIFE CYCLE OF PHARMACEUTICALS



### BACKGROUND AND OBJECTIVE

Increasing supply shortages in Denmark and across the Nordic countries were the background for piloting a joint procurement.

There was a need for solutions to supply issues in Denmark, Norway and Iceland.

One observation was that size of market and the consequence of being a small-volume market impacted efficient competition for older products.

Partner countries in the Nordic alliance decided to pilot joint procurement of older pharmaceuticals.

### METHODOLOGY

- Mapping synergies and differences between Nordic partners
- Profiling products by using the Product Life Cycle model supported identification of relevant pharmaceuticals
- A joint procurement pilot was set up between the countries and led by Amgros, a national procurement organisation

- A political framework agreement was signed between the countries for shared foundation
- The design was tested during the design phase with all the parties involved
- A consultation with the suppliers was established to modify the tender materials

### CONCLUSIONS AND LESSONS LEARNED

- Announced tender criteria were either price alone or price in combination with qualitative criteria
- One of the tenders included a mandatory bid for all three markets, the rest of the tenders were mandatory for Denmark and Norway with optional submission for Iceland
- The complexity of including more markets was countered by the supplier options of delivering to more markets
- Evaluation of the submissions to the pilot showed that a majority of joint tenders had efficient competition with a representative amount of suppliers bidding
- It took two years from start to announcement of the tender
- A key conclusion, is the need for collaboration with stakeholders and collection of proper insights from involved parties prior to announcement of tender

### NEXT STEPS

- A joint evaluation of supply compliance within the tender agreement period will be performed
  - Improvement in supply situation will be tracked during pilot evaluation period
  - Future logistic challenges and strategic solutions to these will be assessed in the early tender planning phase for any future joint procurements
- Questions on Joint Procurement Pilot?  
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# BARRIERS TO ACCESS TO MEDICINES:

- *In rural area:* distance and travel cost to health facility/pharmacy, the amount paid and lack of willingness to pay for medicines; frequently lack of necessary medicines in nearest pharmacy; cost of medicines; quality of purchased medicines; forgetting the way of medicines administration; lack of therapeutic effect after medicine administration
- *In urban area:* the amount paid and lack of willingness to pay for medicines; frequently lack of necessary medicines in nearest pharmacy; cost of medicines; quality of purchased medicines; lack of therapeutic effect after medicine administration.

## ADDRESSING ACCESS BARRIERS TO MEDICINES IN REPUBLIC OF MOLDOVA

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### BACKGROUND

- In middle- and low-income countries average availability of medicines is 35% in public facilities and 66% in the private sector [1]. Cost of medicines and health services remain one of the most tangible households' expenditures in Republic of Moldova.

### OBJECTIVES

- To evaluate barriers in access to medicines in Republic of Moldova (RM) using four access dimensions: geographic accessibility, availability, affordability and acceptability [2].

### METHODS

- A quantitative cross-sectional observational study was conducted through a sociological survey, regarding the access of the population of the Republic of Moldova to the medicines. The study was carried out at the national level, in the Republic of Moldova (2018 year), WHO EURO region.
- A sample of 400 people was selected. 302 answers were validated, 45% of respondents was from rural area and 55% from urban area, from which 64% was women and 36% men.



Figure 1. Four dimensions of the barriers for access to medicines

### RESULTS

- Access was evaluated through four dimensions: geographic – service location and distance; affordability – cost of service and willingness to pay; availability – health workers, medicines, and acceptability characteristics of health/pharmacy services, user attitude and expectations.
- **Geographic:** 24% of population must get to nearest pharmacy and health facilities 30 minutes, between 40%-44% more than 1 hour; 44% have direct distance, in km, to the nearest pharmacy more than 1 km, 24% from rural area must travel more than 5 km to pharmacy. The nearest health facility is at >1km distance for 69% , and 42% from rural should travel >5km.

### RESULTS

- Majority of population get medical facility by walking – 46% from which 22% are rural and 65% from urban area; going to pharmacy walking was mentioned by 58% of people (76%-urban and 35%- rural), at the same time in rural area is more characteristic use of private transport to arrive at pharmacy - 47% and health facility - 52%. The most expensive travel cost is for rural population, 35% of them spend 30-100 MDL (1€=19.8492 MDL), only 8% of urban population spend the same amount. Majority of people prefer to walk to health facility (58%) and to pharmacy (50%).
- **Affordability:** according to results of study 39% (38% urban and 41% rural) of population pay between 101-500 MDL for medicines and 41% (31% urban and 53% rural) for health services in the last month. People that pay 501-1000 MDL for medicines was 23% (14% urban and 34% rural), for health service only 8,6% (8% urban and 9% rural) mentioned that amount, to remark that 36,9% of urban population indicated that they didn't pay for health services. *Willingness to pay was evaluated using Wilcoxon test*, comparing 2 variables: influence of the monthly average amount paid by patient (AAPP) for medicines/health services and willingness to pay for them. AAPP for medicines was 426 MDL, willingness was 292 MDL; AAAP for health service was 327 MDL, willingness was 238 MDL. The value of the asymptotic significance was less than 5% for medicines, thus, have concluded that the amount paid has a strong influence on the amount available for payment, the last one being much smaller. The Wilcoxon test for medical services did not determine an influence - the value of asymptotic significance being >6% (figure 1).
- **Availability:** satisfaction through service in health facility was acceptable for 56% of population, unacceptable only for 7%; for pharmacy service satisfaction was good for 34% of consumer, only 4% wasn't satisfied. 70% of questioned mentioned that they have to wait 1-5 days, from the appointment to doctor's visit. Majority of respondents, 57% remark about supplementary waiting time to get doctor visits from time scheduled, in pharmacy people wait 2-5 minutes to receive counselling by pharmacist, but pharmacist (58% of them) has a neutral attitude to the interests of patients. Only 53% of respondents said that they found needed medicines in pharmacy every time, 47% get them rare, very rare or never.
- **Acceptability:** The main cause that impede purchase of medicines was: cost of medicines in 85% rural and 80% urban population; quality of medicines was in 38% rural and 40% of urban population; remote pharmacy location in 25% rural and 15% urban cases. Weren't selected as an obstacle to medicines use: quality of health/pharmacy service and health facility location. The answer *"I do not permanently purchase all the necessary medicines"* was selected by 92% of rural and 89% of urban population. Factors that restrain medicines use was: *forgetting the way of administration in 59% of rural and 30% of urban population*; lack of money for a treatment cure 32% of rural and 39% of urban patients.

### CONCLUSION

- To address barriers health system should ensure health equity, universal health coverage, provision of essential medicines and health care services, pay for performance and a good regulatory approaches using needs-based financing.

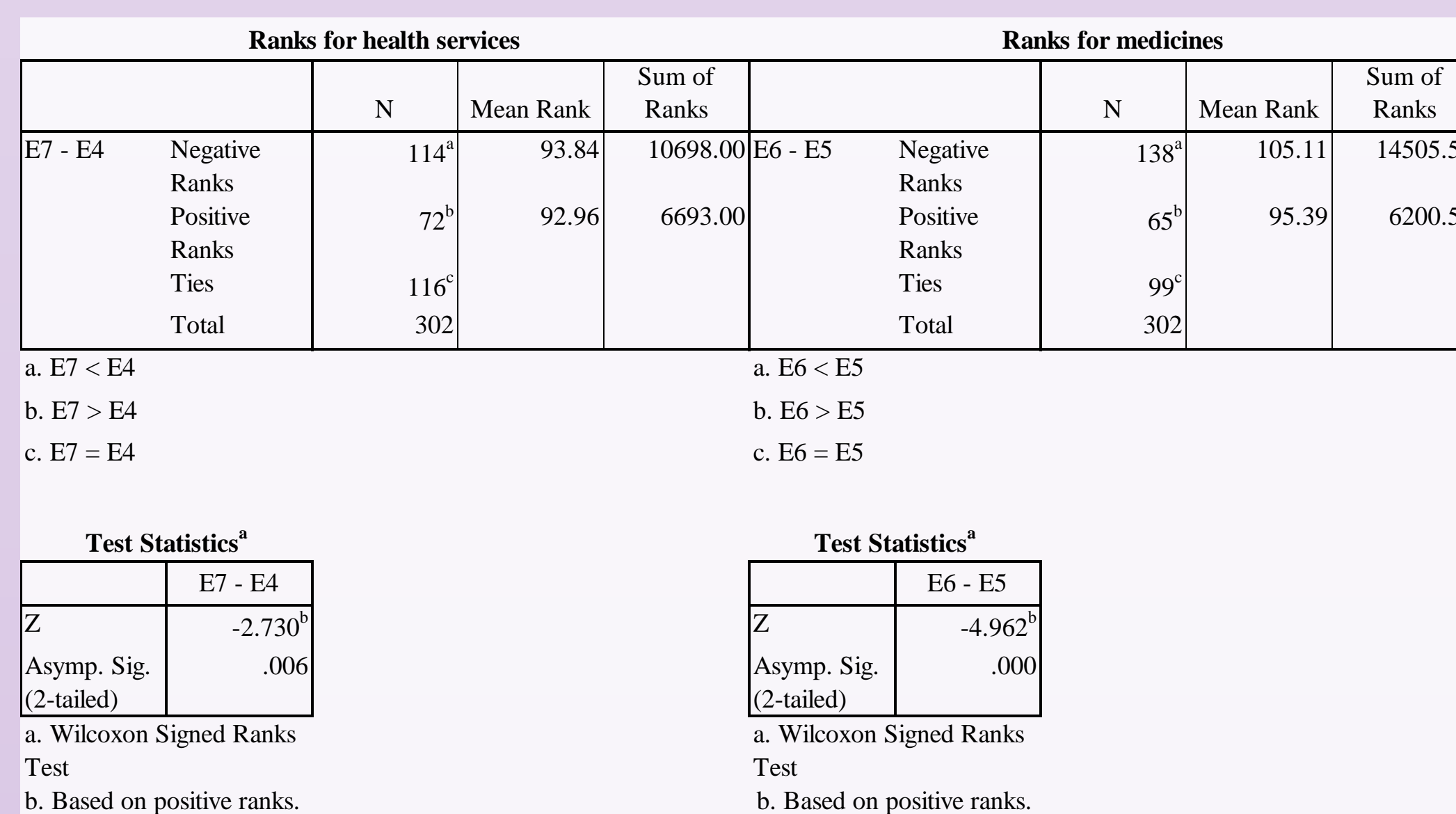


Figure 2. Willingness to pay was using Wilcoxon test for medicines and health services

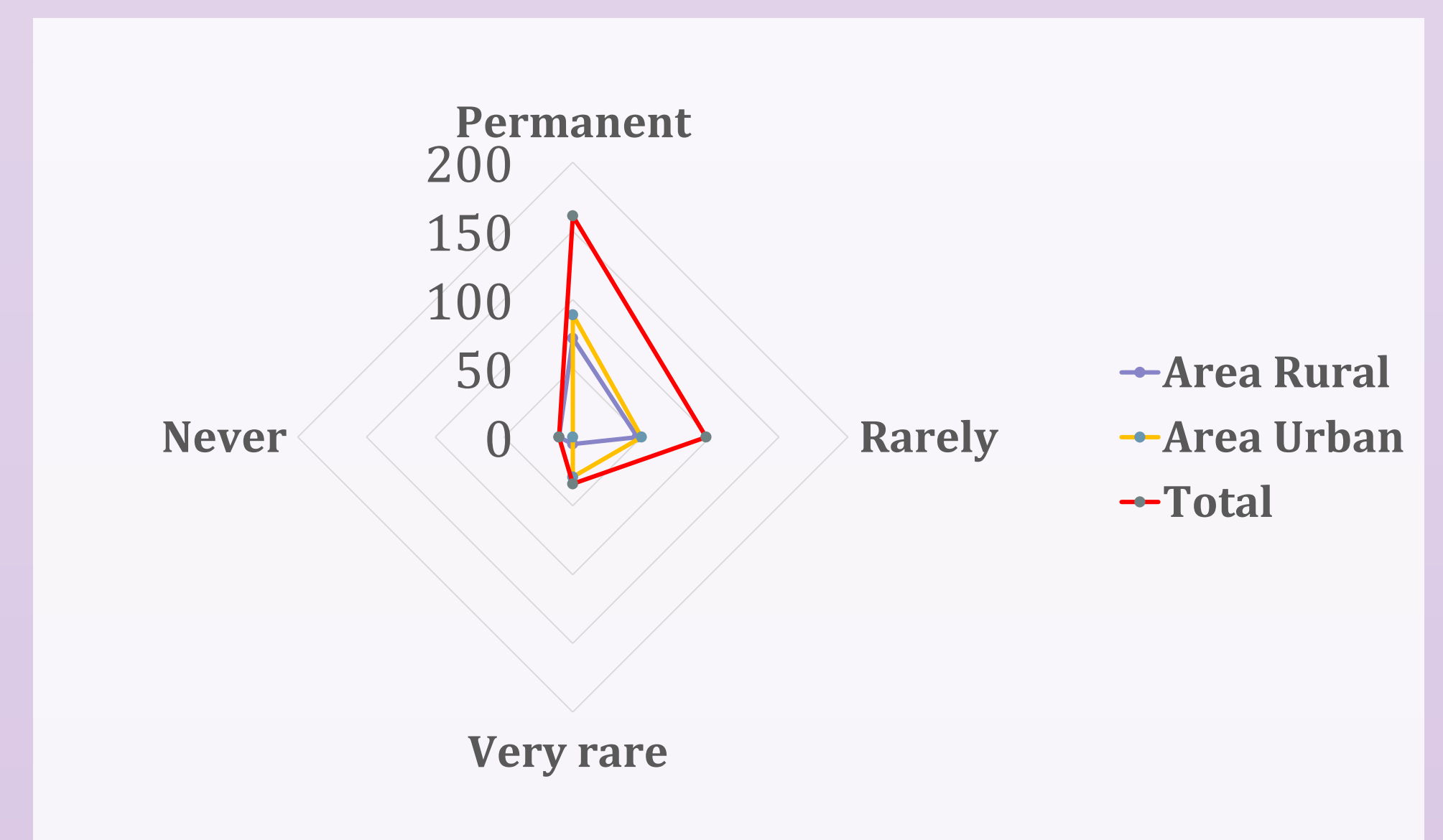


Figure 3. Frequency of the presence of the necessary drugs in the pharmacy

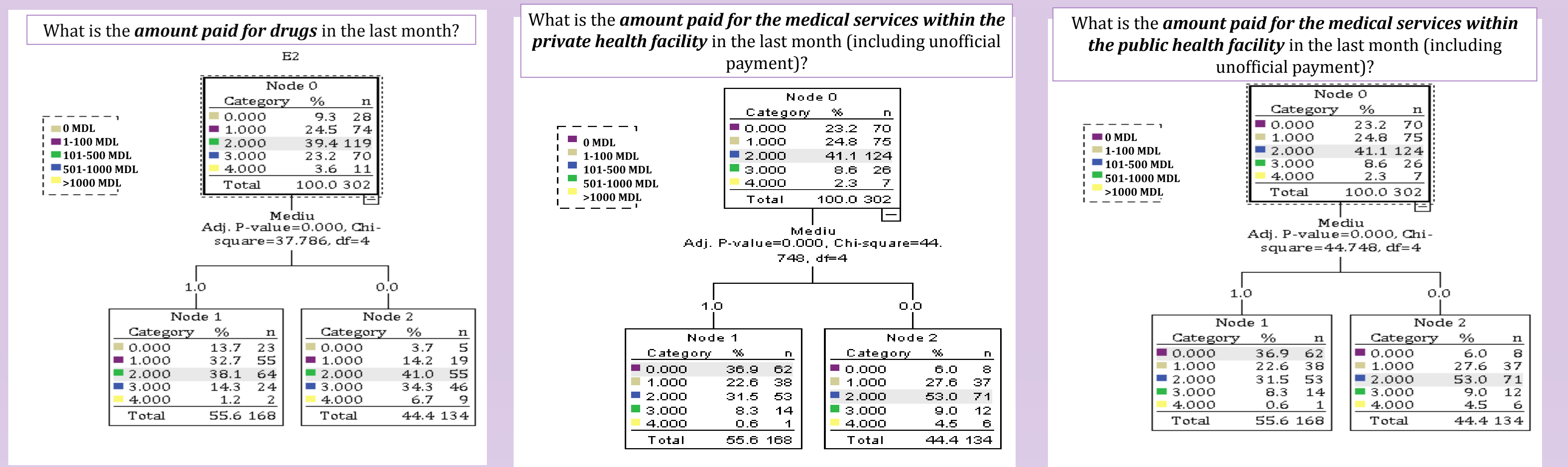


Figure 4. Affordability test for medicines and health services



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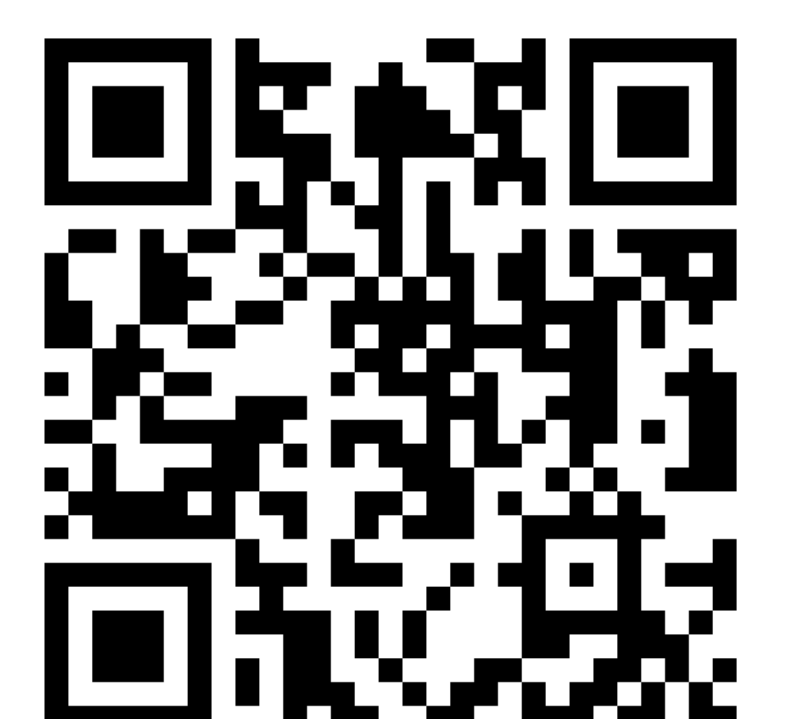
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# The rising costs of Orphan Drugs in Italy

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2 - WHO Collaborating Centre for Pharmaceutical Policy and Regulation, Utrecht University, The Netherlands  
3 - AXES research unit IMT School for Advanced Studies, Lucca, Italy  
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## Background

Orphan Medical Products (OMPs) are drugs intended for the treatment of serious conditions affecting less than 5 in 10,000 people in the EU.

OMPs have brought a huge contribution in many areas that had been orphan in therapeutics for a long time, improving the quality of life and the life-expectancy of patients.

On the other hand, although the ‘orphan’ designation allows applicants to benefit from incentives and conditional marketing authorization by the EMA to sustain their development, the prices of some these are very high and the increasing number of OMPs marketed every year has challenged the sustainability of the pharmaceutical expenditure.

## Objectives

This paper aims to give some insights into the Italian Pricing & Reimbursement Policies on OMPs highlighting the strengths and weaknesses of the system.

## Methodology:

**Data source:**  
Pharmaceutical Expenditure  
Pricing & Reimbursement policies and procedures  
Legal framework

**Region covered:** Italy  
**Time period:** 2017



## Conclusion

**In Italy the policies on OMPs are largely inclusive:** the National Healthcare System allows the access to these drugs even before standard marketing authorization through special pathways.

Orphan drugs are allowed flexibility in the grade of assessment to get the innovative status: a) **specific early access programs**, b) they were **not affected to payback** by the pharmaceutical companies, should the drugs budget be overrun.

Incentives provided at EU level, along with the status of innovative granted by the AIFA – even in presence of moderate or low level of evidence - were set up to **sustain the survival of OMPs, not to make some of them the new blockbusters.**

## References

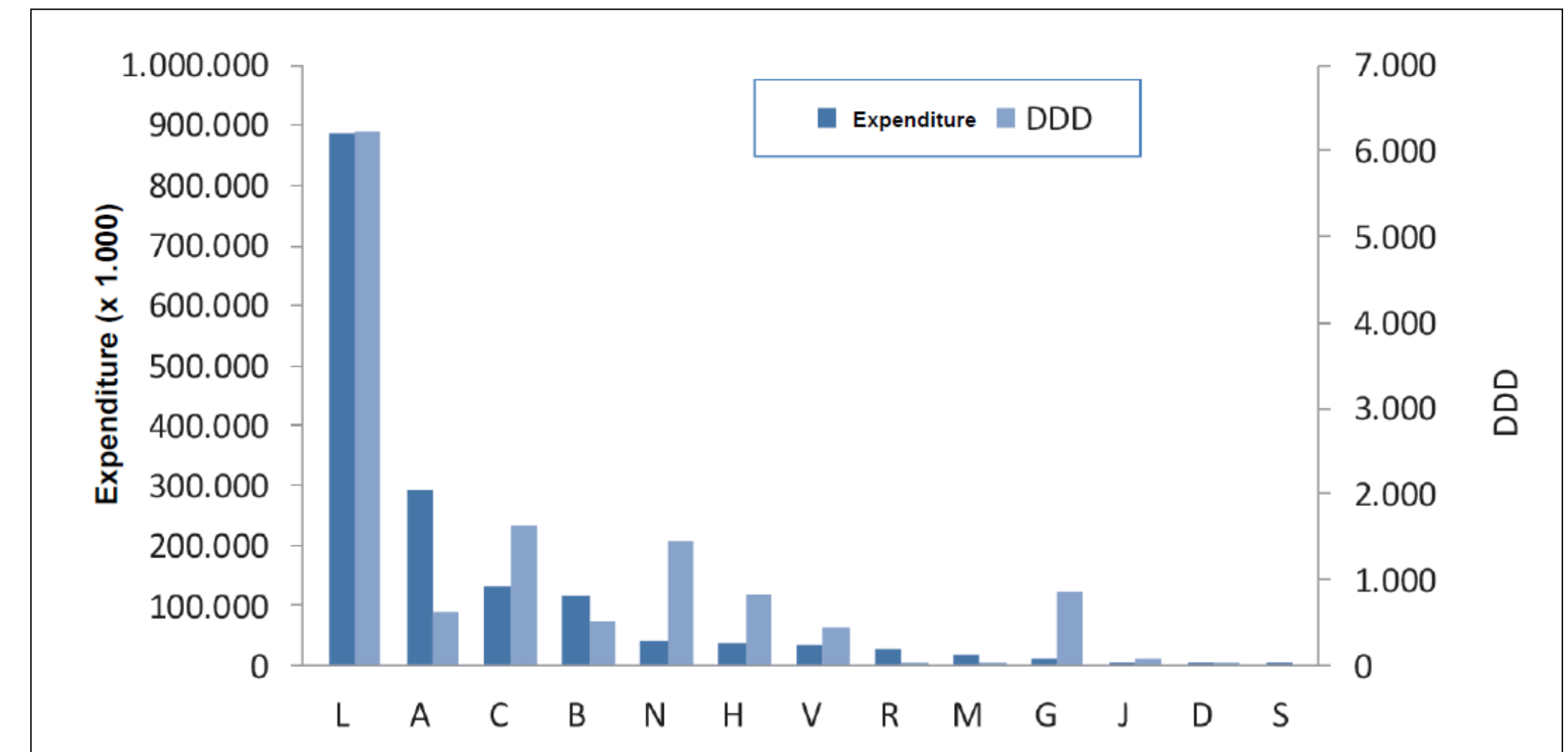
The Medicines Utilisation Monitoring Centre. National Report on Medicines use in Italy. Year 2017. Rome: Italian Medicines Agency, 2018.  
Available from: [www.aifa.gov.it](http://www.aifa.gov.it)

## Results

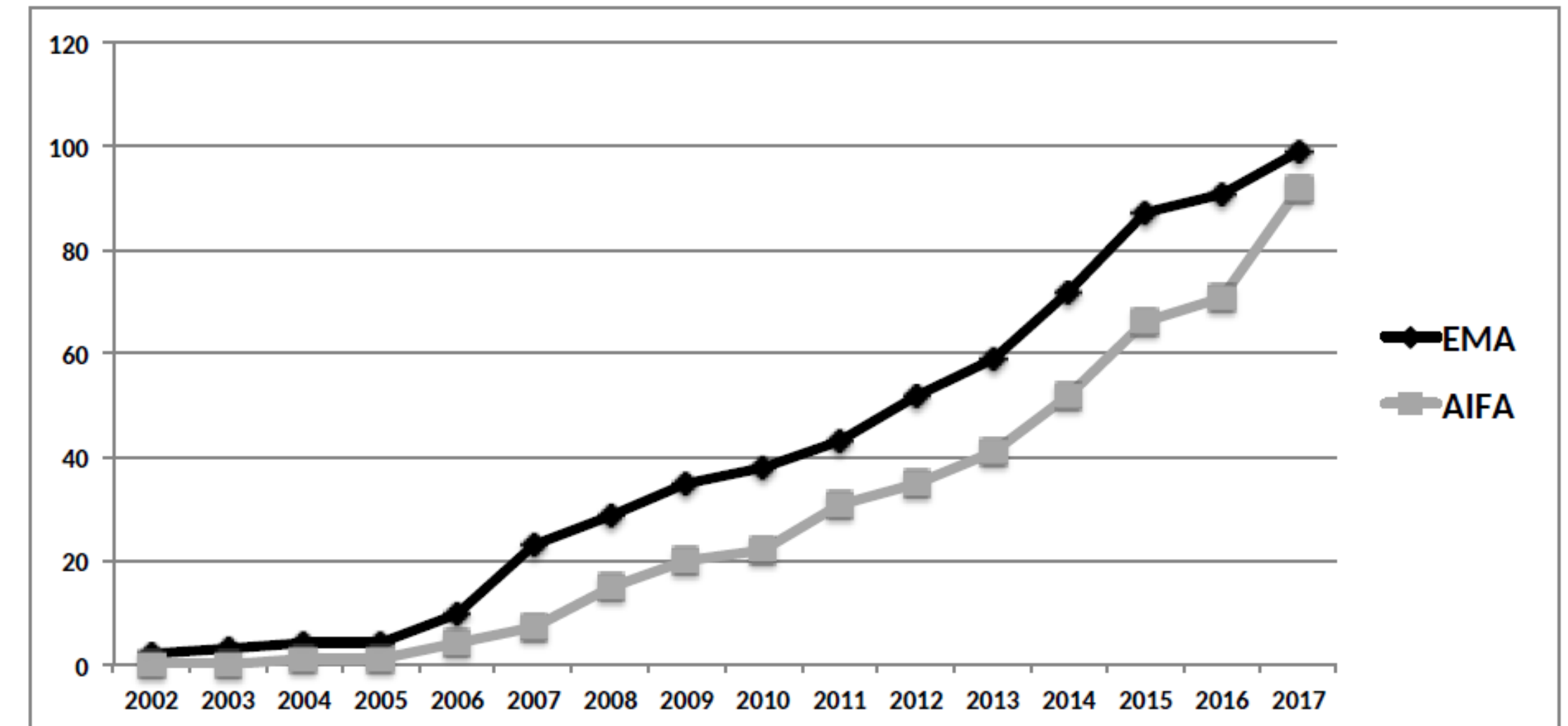
In Italy the expenditure for OMPs increased from €652 millions in 2010 (3.5% of the whole public Pharmaceutical Expenditure) to €1,599 millions in 2017 (7.2%).

Year	2010	2011	2012	2013	2014	2015	2016	2017
OMPs expenditure	657	800	671	917	1.060	1.212	1.393	1.599
% OMPs expenditure	3,50	4,20	3,50	4,67	5,31	5,49	6,13	7,20
OMPs DDD	6,6	7,5	5,9	7,5	8,5	10,3	11,4	12,7
% OMPs DDD	0,03	0,03	0,02	0,03	0,03	0,04	0,04	0,05

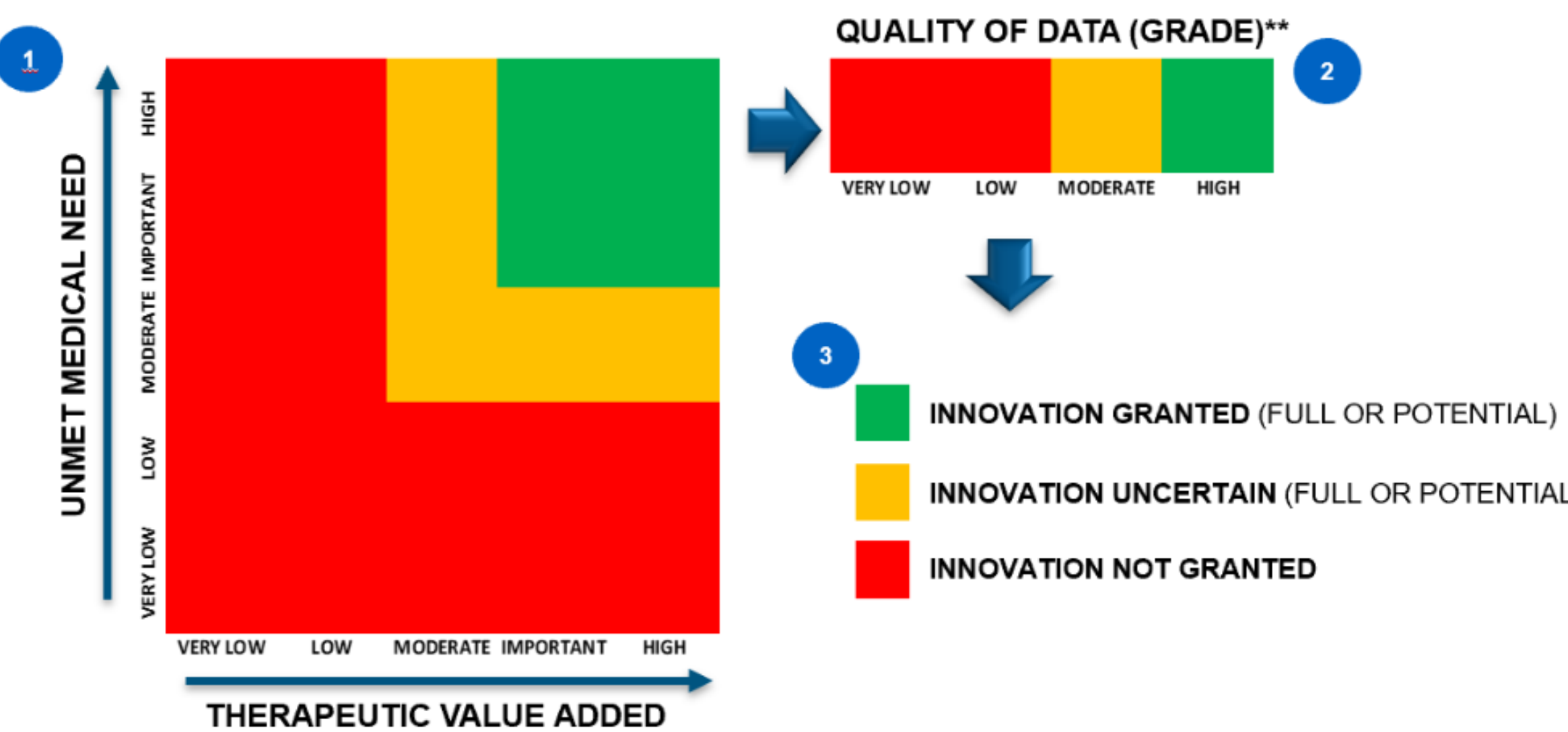
Some OMPs are ranking within the first 30 top-selling drugs. Drugs for cancer and haematological malignancies account for an important proportion of pharmaceutical expenditure for OMPs



Out of the 99 OMPs authorized by the EMA, 85 were reimbursed by the AIFA. The remainders were either marketed though temporary not-reimbursed or accessible through law 326/2003 (AIFA 5% Fund), which provides the reimbursement of not-yet-marketed OMPs through a fund financed by the 5% of annual expenses for the promotion activities of the pharmaceutical companies. In 2017 the AIFA fund supported the access to 13 OMPs for 40 patients (€13.465.742).



AIFA may grant a medicine the status of innovative drug according to 3 criteria: unmet medical needs, clinical added value and quality of evidence. This allows access to special funds, exemption from payback mechanisms and the immediate availability at local/regional level.



Unlike non-orphan drugs - where high-quality of evidences are required - OMPs may be granted the status of innovative also when the level of evidence is moderate or low.

**Keywords: Orphan Drugs, rare diseases, affordability**



# Price Realignmentments and Commercial Agreements have resulted in significant savings to the HSE, albeit at the expense of transparency of prices

## An Examination and Assessment of the Processes Involved in Setting Reimbursement Prices for Medicines in Ireland

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### Background

The Irish Health Service faces significant future challenges with growing costs of new medicines, combined with a pipeline of highly expensive medicines. Non-transparent commercial arrangements have helped manage the adoption and funding of expensive medicines. The 2016 IPHA Framework Agreement between the State and Irish Pharmaceutical Healthcare Association (*IPHA*), was anticipated to achieve significant savings, in part through Schedule 5 which ensures that list prices of all medicines will be realigned, downwards only.

### Objective

This study examined processes involved in setting reimbursement prices for new medicines whilst determining the financial benefits from having an assessment and commercial negotiation process. The extent to which price realignments over time improved transparency of commercial arrangements and the long-term commercial impact of commercial negotiations at application stage were assessed. This study sought to assess whether or not there are more appropriate or efficient means of setting reimbursement prices for medicines in Ireland, determining if and what the financial benefits of the overall processes are and addressing the benefit of offsetting the transparency of pricing in favour of achieving savings.

### Methods

A literature review was completed for between 2010, when the first medicine approved for reimbursement with a commercially confidential agreement was applied for and 2018, to collect information on reimbursement processes and the use of commercially confidential agreements across the EU. 25 medicines with commercially confidential agreements were examined. Letters of approval, commercially confidential agreements, price and application forms, rapid review documents, health technology assessment reports and summaries and communications between manufacturers and the CPU were analysed. Annual realignments as per Clause 5.2 of the IPHA Framework Agreement were analysed.

### Results

From a sample of 25 commercially confidential agreements, commercial discounts ranged between 5% and 60%. Agreements consisted of budget caps, discounts off list prices and tiered discounts. Most agreements included discounts off the list price collected through rebates. Forecasts estimated commercial agreements to last from less than 500 days to almost 3500 days. The majority (72%) of medicines realigned downward in price annually, in 2016, 2017 and 2018. 12% (n=3) of medicines have realigned below their non-transparent commercially agreed price. The average time taken to reimbursement decreased year on year. For the 25 medicines examined, savings resulting from non-transparent commercially confidential arrangements total approximately €50 million to date.

### Conclusions

Annual realignments and commercial arrangements have proven beneficial to the Irish State with significant savings made. CPU has played an integral role in negotiating confidential agreements with pharmaceutical companies. Transparent pricing would be preferable but is challenging given international reference pricing constraints. The process for setting reimbursement prices in Ireland is robust and this study goes some way to support that. Nevertheless, with significantly greater challenges expected in future, additional measures are required.

Table 1: Therapeutic areas analysed medicines are used to treat	
Therapeutic Area	Number of Medicines (%)
Cancer	15 (60)
Chronic thromboembolic pulmonary hypertension (CTEPH) / Pulmonary Arterial Hypertension (PAH)	1 (4)
Epilepsy	1 (4)
Human Immunodeficiency Virus (HIV)	1 (4)
Immune thrombocytopenic purpura (ITP)	1 (4)
Multiple sclerosis	2 (8)
Myelofibrosis	1 (4)
Psoriasis	1 (4)
Rheumatoid arthritis	2 (8)

Figure 1 Therapeutic areas of medicines with commercially confidential agreements

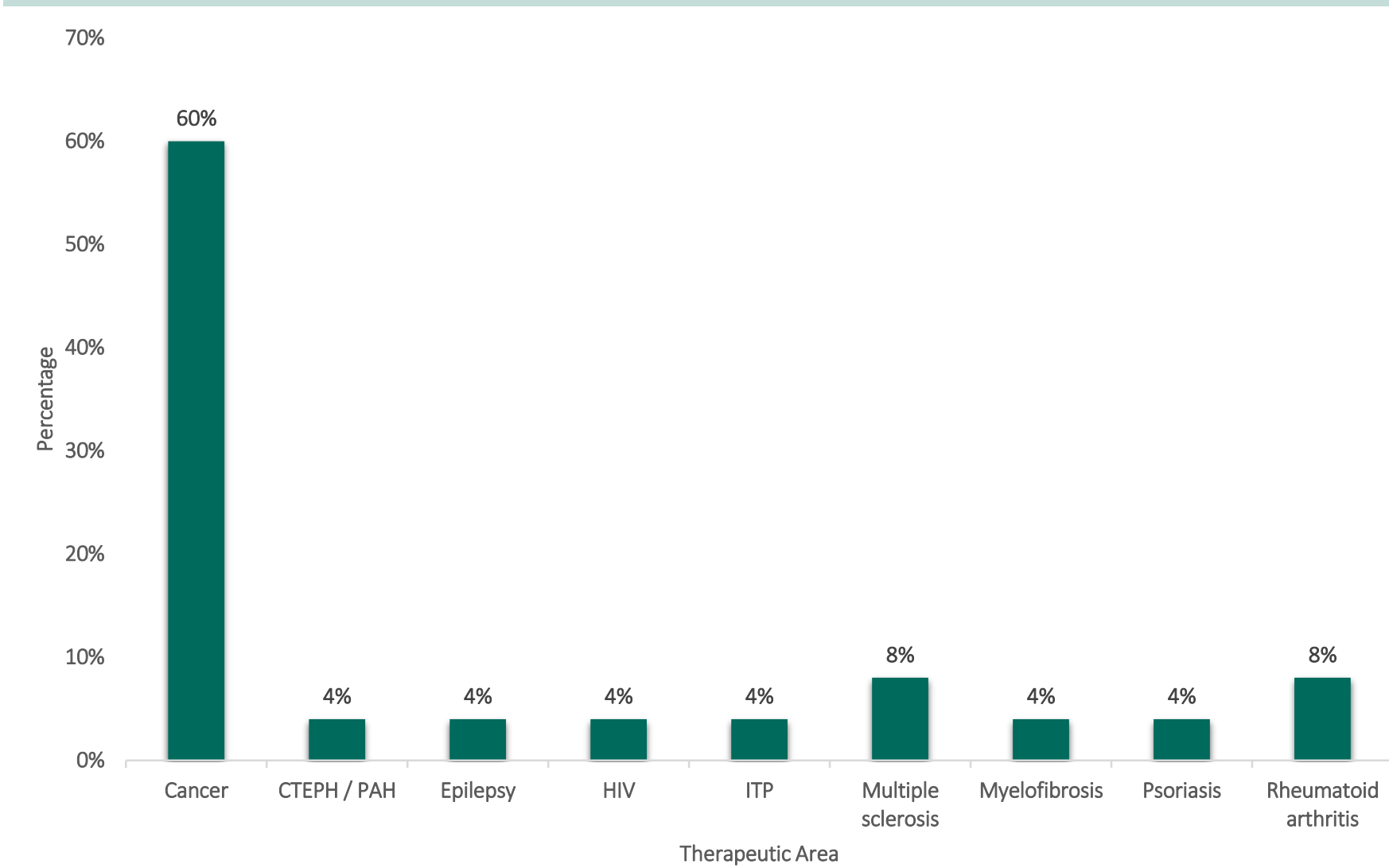


Figure 3 Time taken between date of initial application and date of approval for reimbursement

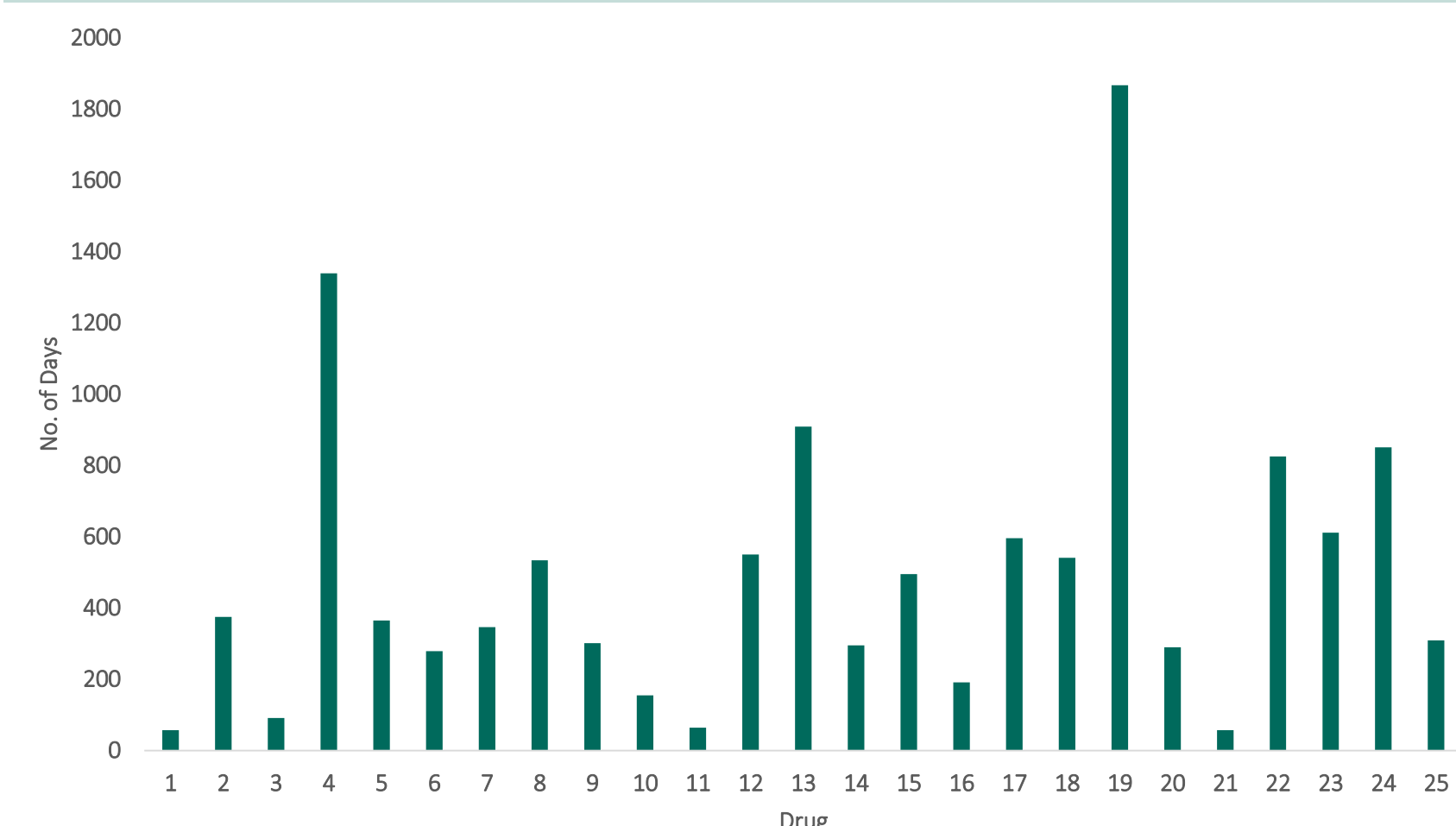


Figure 5 Length of agreed duration of commercial in confidence agreements (Years)

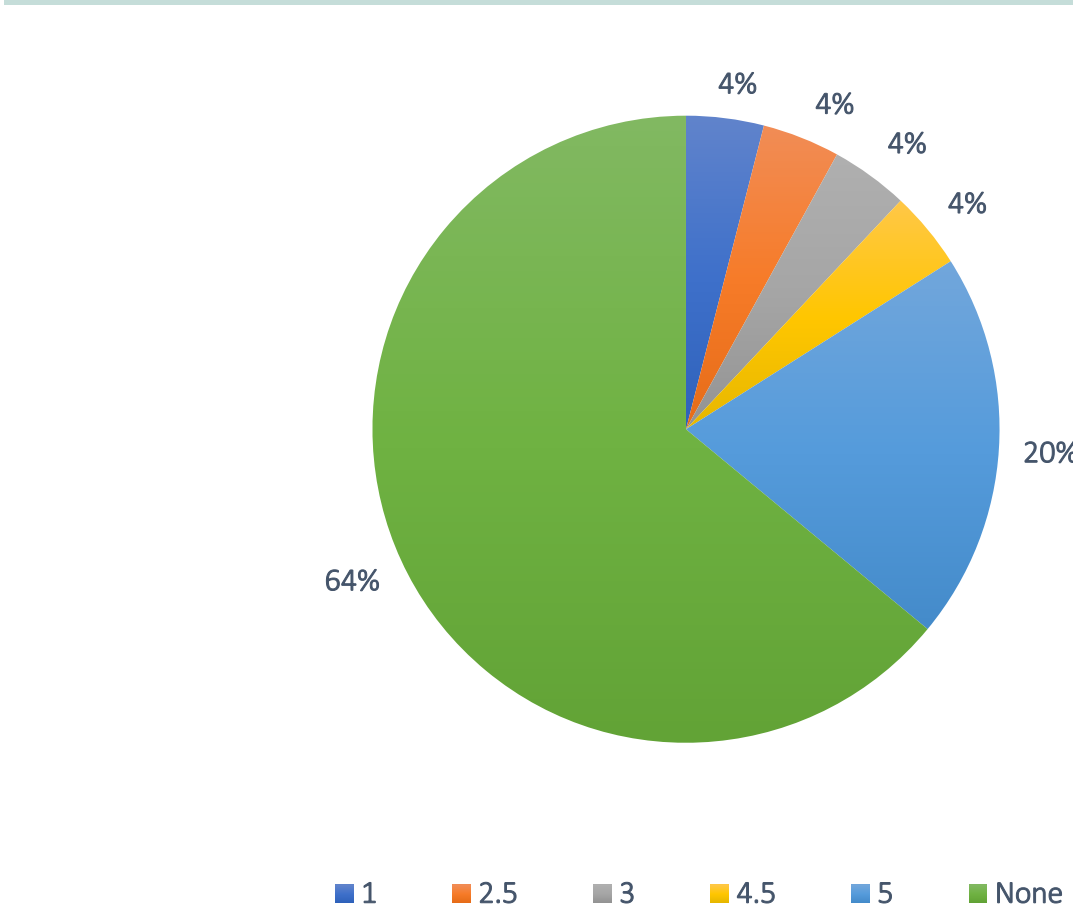


Figure 7 Percentage of medicines with prices realigned below non-transparent price

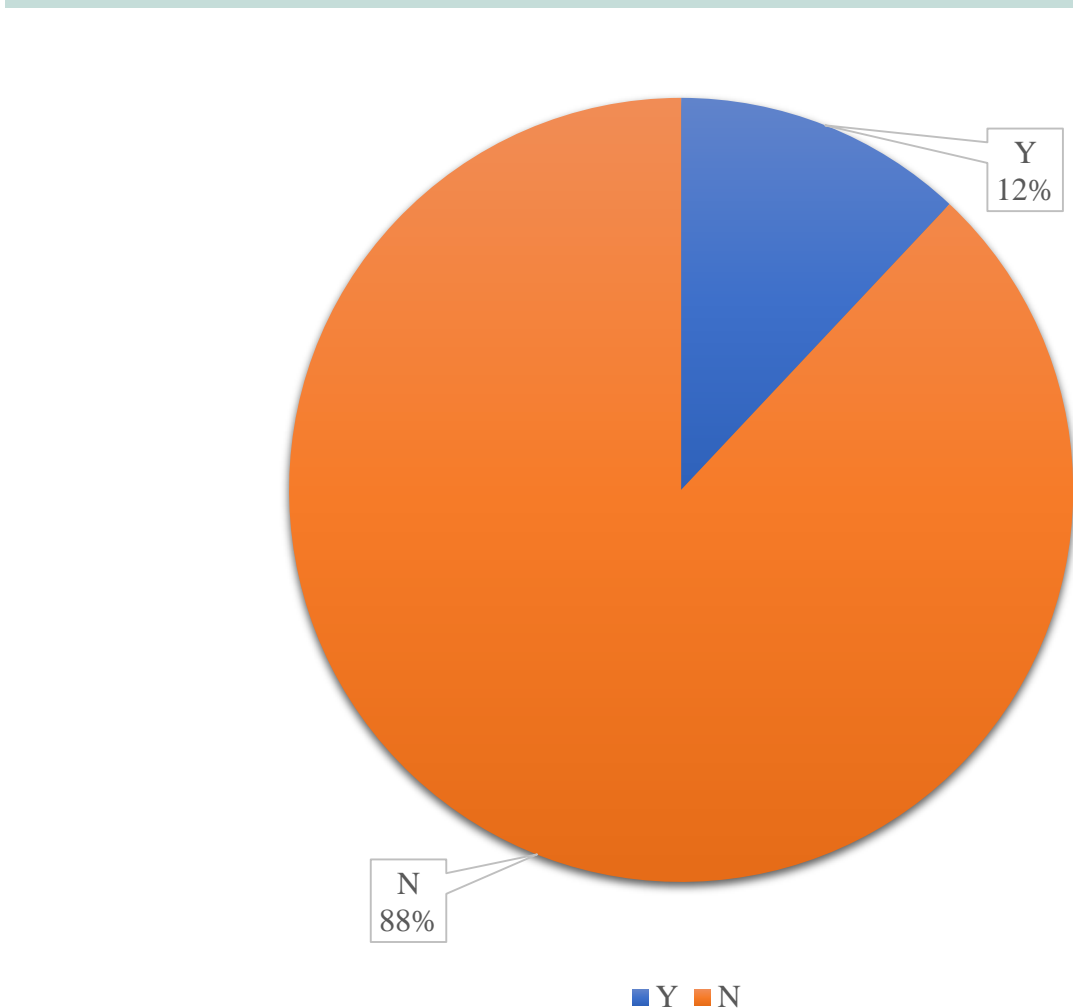


Table 2: Schemes through which medicines are reimbursed	
Scheme	Number of Medicines (%)
GMS	1 (4)
HTDS	16 (64)
ODMS	7 (28)
Hospital	1 (4)

Table 4: Percentage of agreements with an agreed duration		
Agreed Agreement	Duration of Agreement	Count of Drug (%)
Y		9 (36)
N		16 (64)

Figure 2 Percentage difference between initial price on application and agreed non-transparent price

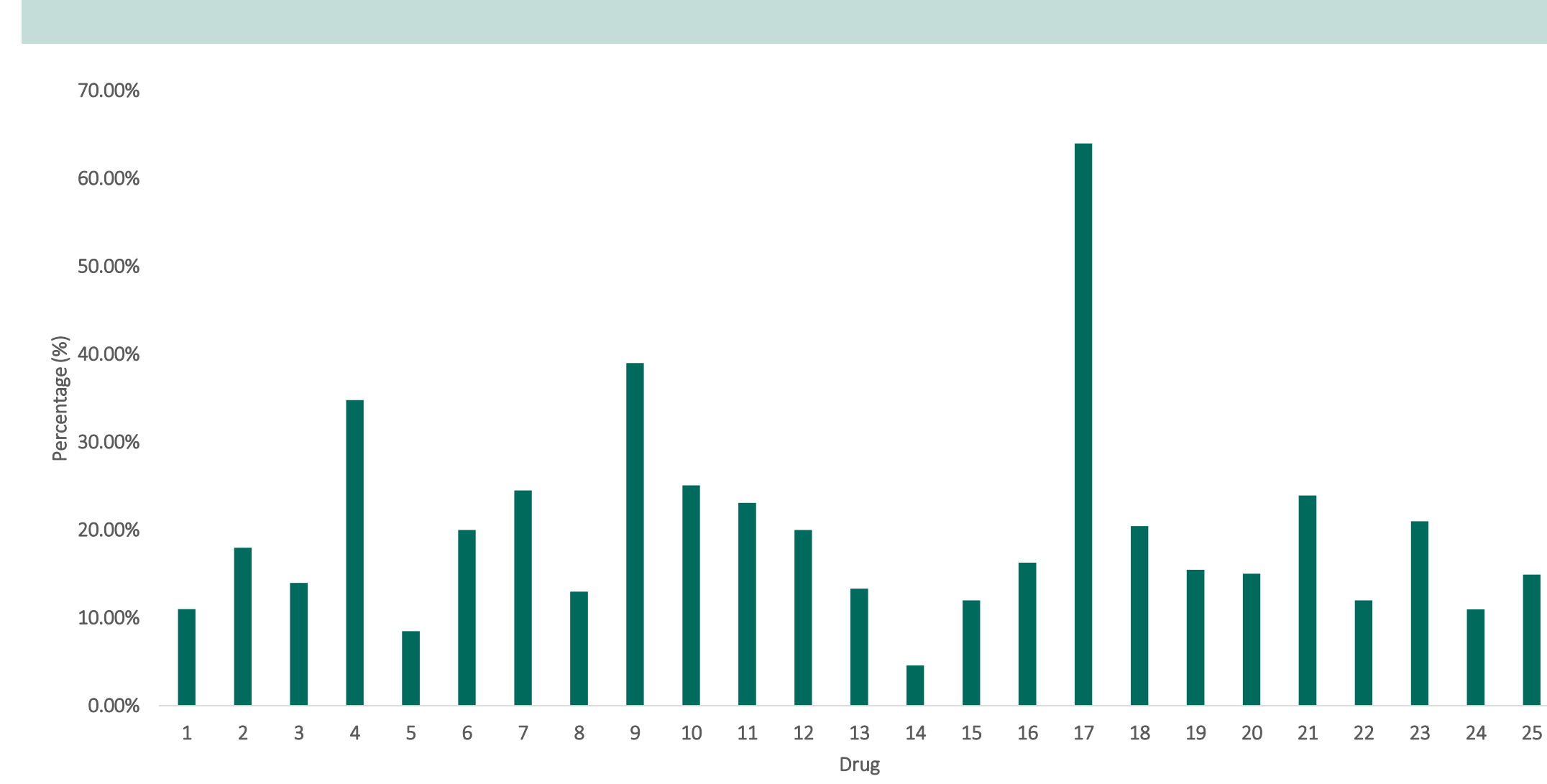


Figure 4 Average time taken from date of application until approval for reimbursement



Figure 6 Percentage of drugs whose prices had realigned downwards

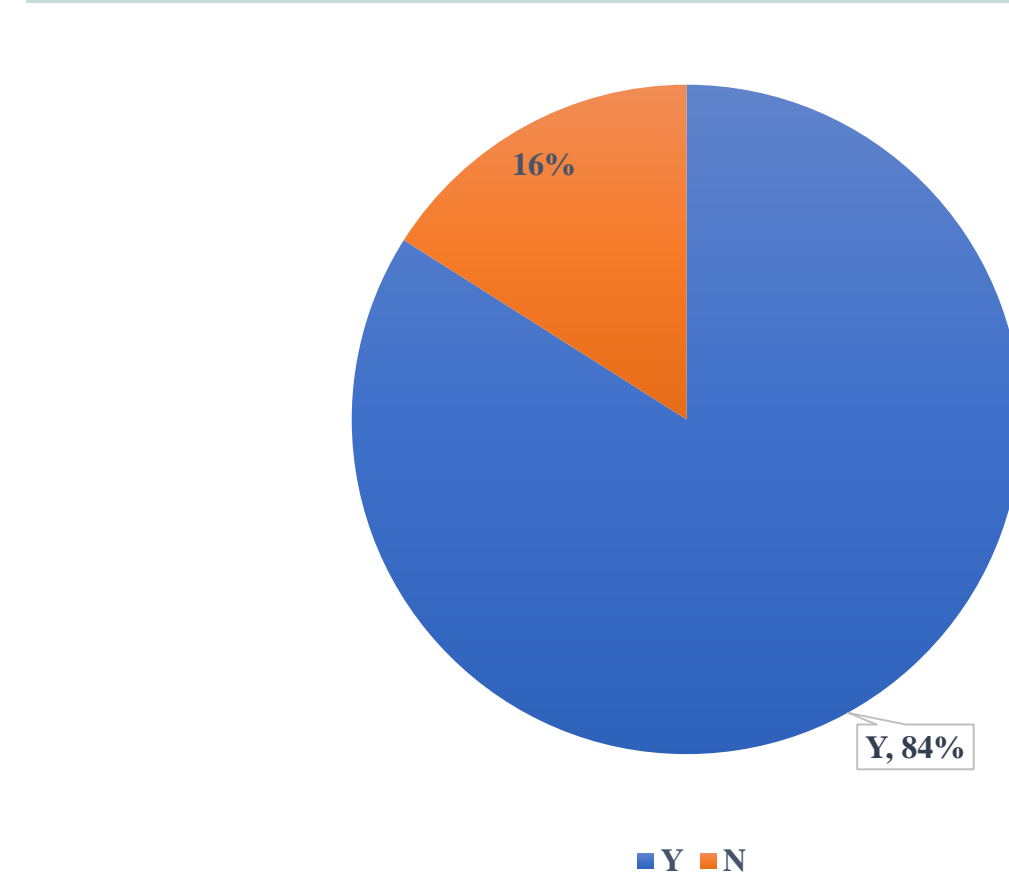
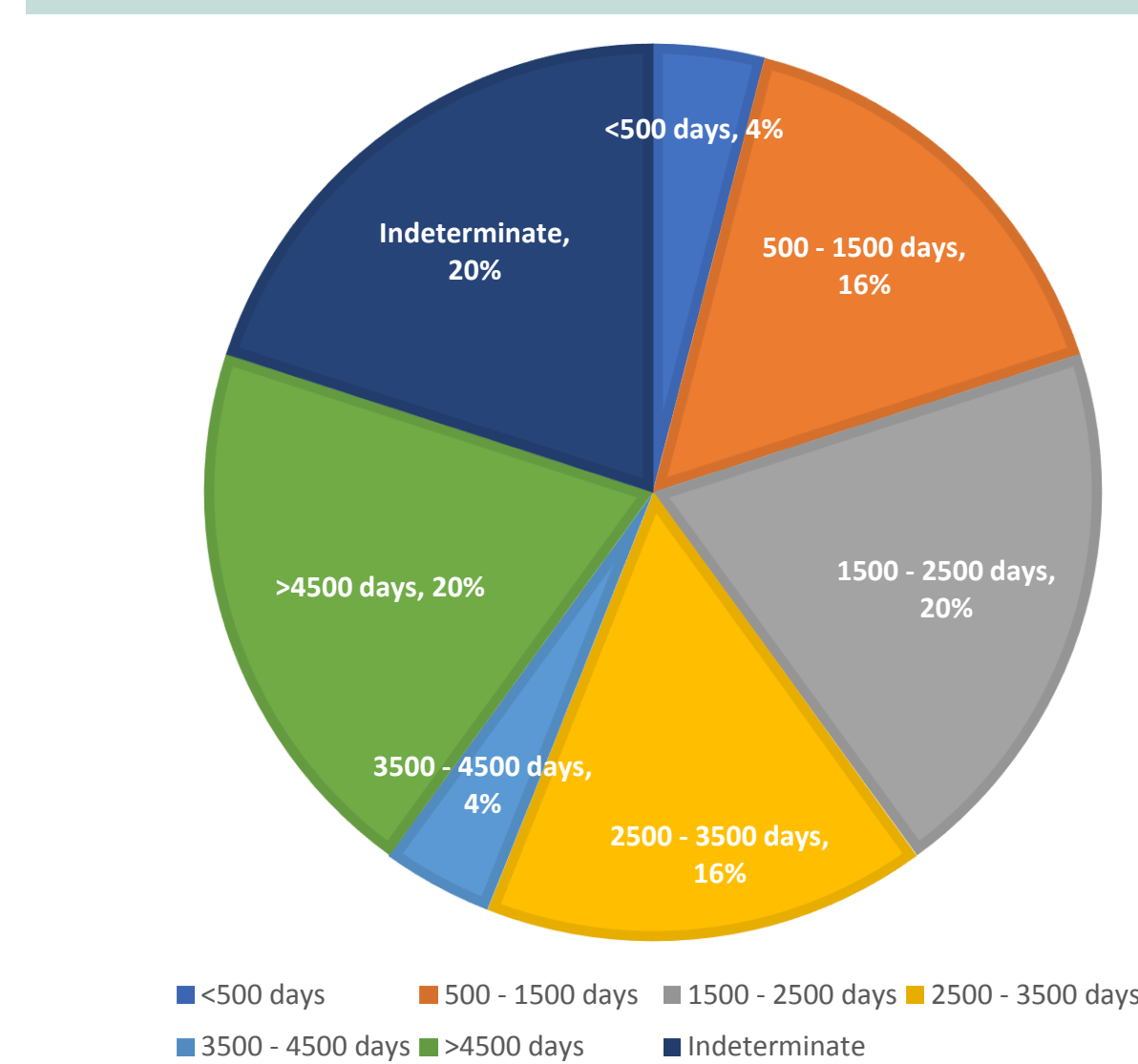


Figure 9 Forecasted durations of confidential agreements





# Innovative policies to achieve sustainable drug prices – a literature review

The objective of this study was to facilitate an evidence-based discourse on innovative policy options to reduce drug prices at market launch. We reviewed the literature to make an inventory of options, analyzed the underlying evidence, and selected promising policies.

**Background:** Access to medicines is essential to secure people’s right to health. High expenditure on novel anticancer drugs threatens this right and, considering finite resources, the financial sustainability of care. Innovative solutions are needed and highly discussed.

**Methodology:** We performed a systematic scoping review to identify policy options to reduce drug prices at market launch that are relevant to oncology and high-income countries. We inventoried policy options, categorized publications based on evidence, and analyzed quantitative articles. To select promising options, we identified main price mechanisms, rated policies based on their system disruption and potential price impact. Finally, we asked European experts in the field of oncology and health regulation to rate proposals and challenge our selection of promising policies.

*Region covered:* We screened globally and selected for the EURO region. *Time period:* 2001-2019

**Results:** We screened 4775 articles and selected 80 articles that we used to produce an inventory of policy options in the intellectual property, pricing, and the research & development environment. 22 articles used a quantitative approach but, overall, there was low available evidence. We identified promising options of which experts prioritized transparency and combined purchasing. Two-part-pricing and de-linkage were the most controversial policies.

**Conclusions and lessons learned:** Although it is important to reform pharmaceutical regulation to secure access to medicines, a coordinated approach to structurally evaluate proposals is lacking. Quantitative methods are rarely used, and current evidence is insufficient to structurally evaluate proposals. We advise testing proposals with small-scale experiments, dynamic simulations, and pilots.

## Classification of included articles according to their evidence


Evidence		Study type	IP Pricing R&D Mix Total				
Quantitative	Empirical	Policy evaluation	1	1			2
		Market dynamics evaluation		4	3		7
	Mathematical	Dynamic, numerical	2				2
		Static, numerical	5		1		6
		Static, abstract		6			6
Subtotal			8	11	4	0	23
Qualitative	Conceptual	Framework to score policy options	1	1		1	3
		Systematic review				3	3
		Theoretical model	10	4	4		18
	Opinion	Perspective	11	9	7	6	33
Grand total			30	25	15	10	80

## Inventory of policy options


	<div><div></div>= no</div>	<div><div></div>= weak</div>	<div><div></div>= medium</div>	<div><div></div>= strong</div>
Intellectual property	Price mechanism	Evidence	System Disruption	
	Increase competition		Low	
	Earlier generic entry		Low	
			Low	
			Medium	
			Medium	
	Increase competition		High	
	de-linkage		High	
			High	
	Control prices		Medium	
Pricing	Price mechanism	Evidence	System Disruption	
	Reduce prices for subsets of population or drugs		Low	
			Low	
			Medium	
	Control prices		Medium	
			Medium	
	Increase information to improve competition		Medium	
R&D	Price mechanism	Evidence	System Disruption	
	Reduce R&D costs		Medium	
			Medium	
			High	
	Increase competition		Medium	
			High	
			High	
	Recoup investments		Medium	
	Reduce granted benefits		High	

Promising policies to reduce drug prices are: transparency, de-linkage, two-part-pricing, public research, orphan drug reform, and public clinical trials.


There is limited quantitative evidence available. We advise structurally testing policy options with pilots and simulation models.



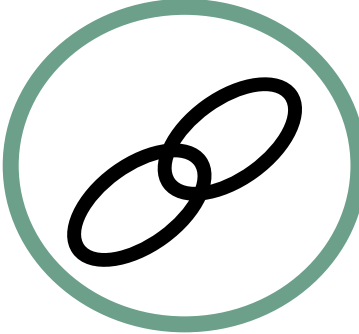
**Transparency:** Public knowledge of drug prices, R&D costs, and /or clinical trial results.




**Two-part-pricing:** A subscription payment method that consists of an entry fee (to access the product) and a small usage fee (per unit sold).




**Orphan drug reform:** Stricter orphan drug regulation to account for often high profitability and for decreasing population sizes with targeted therapies.



**De-linkage:** Decoupling the innovation and the production process. Replacing patents with alternative tools to incentivize innovation.



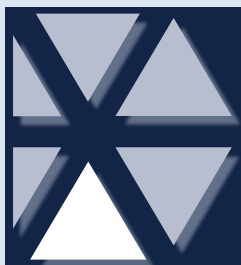
**Public research:** Extending the role of publicly funded research beyond basic research to launch drugs at sustainable prices.



**Public clinical trials:** Installing a public agency to conduct clinical trials and, thus, reduce waste, increase information, and lower the financial barrier of clinical trials.

What is the effect of lower prices on profitability, private investments, and on the innovation pipeline of novel drugs?





# Monitoring evidence on overall survival benefits of anticancer drugs approved by the EMA



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<sup>2</sup> Austria and Lower Austrian Sickness Fund, St. Pölten, Austria

<sup>3</sup> Department of Health Economics, Center for Public Health, Medical University of Vienna, Vienna, Austria

<sup>4</sup> Ludwig Boltzmann Institute for Applied Diagnostics, Vienna, Austria

## Background and project aim

The introduction of fast-track licensing strategies increases the approval of anti-cancer drugs with ambiguous benefit-risk profiles [1]. Thus, in many instances there is lacking evidence about overall survival (OS) at the time of marketing authorisation [2-4]. Our objective was to monitor and characterise therapies with ambiguous benefit-risk profiles and identify any post-approval updates on median OS after at least three years of approval by the European Medicines Agency (EMA).



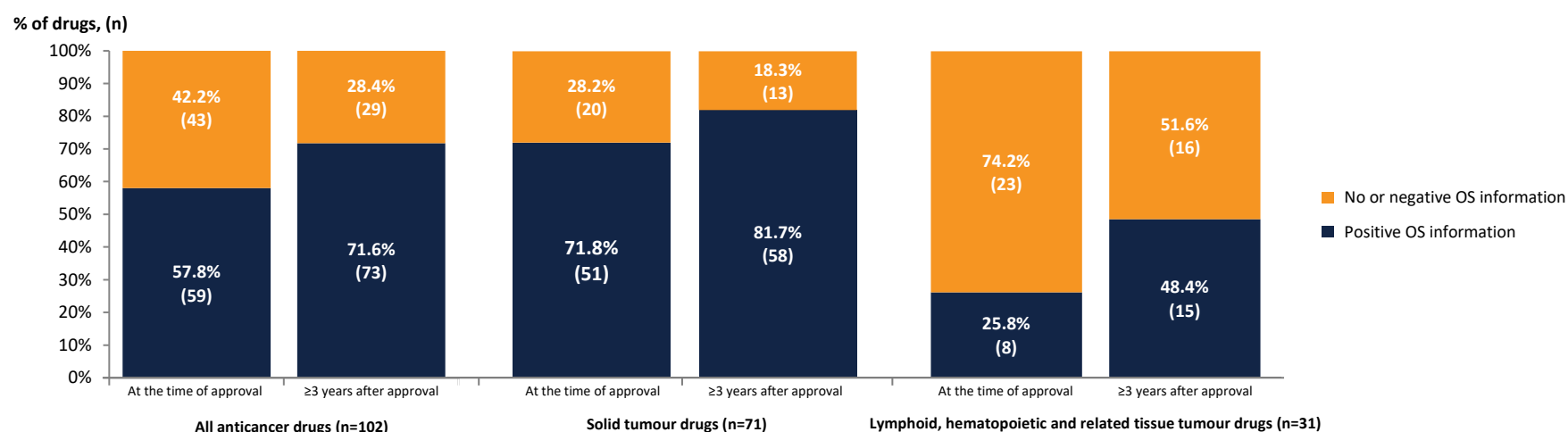
## Methods

In our cross-sectional analysis, we included all originator anti-cancer drugs with initially ambiguous benefit-risk profiles that received marketing authorisation by the EMA between Jan 1, 2009 and May 31, 2015. Our monitoring timeframe for the identification of OS updates was at least three years after EMA-approval. To identify study updates, the following three sources were included: clinicaltrials.gov, EPARs, and PubMed, whereby the terms for the systematic literature search were “(name of the active substance) AND (NCT number OR trial name)” with no further restrictions.



## Results

In total, we identified 102 eligible approval studies. Out of these, a negative difference in median OS or no information was available in 43 (42.2%) instances. During monitoring, 11 updates with accessible information on median OS could be identified. Including monitoring results, there are still 32 remaining therapies (31.4%) where no or negative information (n=27 [26.5%] and n=5 [4.9%], respectively) regarding median OS is present at least three years after EMA approval.



## Conclusion

One-third of oncology drugs with ambiguous benefit-risk profiles fail to demonstrate a survival benefit even after several years of marketing authorisation. Systematic and transparent post-approval monitoring mechanisms will be of high relevance to assure a clinically relevant patient benefit, since the trend towards faster access to medicine with uncertain benefit is increasing rather than declining.

## References

- [1] Vella Bonanno P, Ermisch M, Godman B, Martin AP, Van Den Bergh J, Bezmelnitsyna L, et al. Adaptive Pathways: Possible Next Steps for Payers in Preparation for Their Potential Implementation. *Frontiers in pharmacology*. 2017;8:497.
- [2] Grössmann N, Robausch M, Rosian K, Wild C, Simon J. Monitoring evidence on overall survival benefits of anticancer drugs approved by the European Medicines Agency between 2009 and 2015. *European Journal of Cancer*. 2019;110:1-7.
- [3] Grössmann N, Del Paggio JC, Wolf S, Sullivan R, Booth CM, Rosian K, et al. Five years of EMA-approved systemic cancer therapies for solid tumours-a comparison of two thresholds for meaningful clinical benefit. *European journal of cancer (Oxford, England : 1990)*. 2017;82:66-71.
- [4] Kim C, Prasad V. Cancer Drugs Approved on the Basis of a Surrogate End Point and Subsequent Overall Survival: An Analysis of 5 Years of US Food and Drug Administration Approvals. *JAMA internal medicine*. 2015;175(12):1992-4.





# The experience of the Tuscan Region in managing biosimilar penetration

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## Background

Italy is a leading country in the uptake of biosimilars, with their use been constantly growing; nevertheless, their diffusion is not uniform across Regions. Most Regions have implemented specific policies concerning biosimilar governance to guarantee equity and financial sustainability.

## Objective

Some Italian Regions established policies to promote the entry of biosimilars into the therapeutic plans (i.e. Tuscany); others have drawn up late and unfocused policies having a low penetration of biosimilars (i.e. Lazio).

The purpose of this paper is to investigate which governance tools support a high penetration of biosimilars ensuring equity and financial sustainability.

The case of the Tuscany Region has been developed.

## Methodology

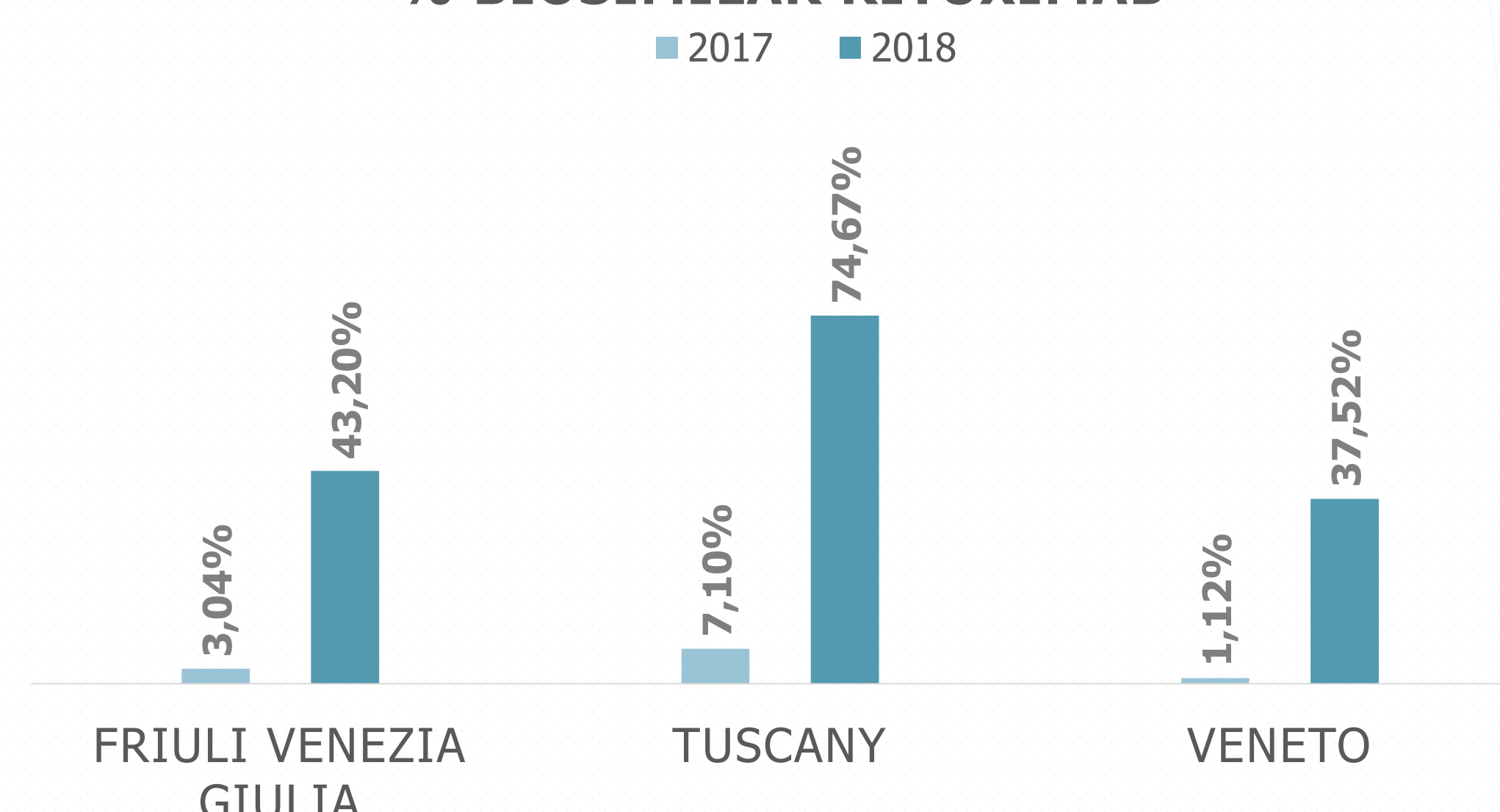
Regional pharmaceutical administrative flows were analyzed to identify the penetration rate of biosimilars in Tuscany.

Molecules with low penetration and high potential for economic savings were selected and a catalogue of indicators for these molecules realized. An engagement process with managers and specialists of Tuscan Local Health Authorities was started to discuss the indicators and define shared targets of increasing the uptake. The engagement process was soon transformed into regular meetings to monitor the achievements, benchmark against each other and revise objectives.

## Results

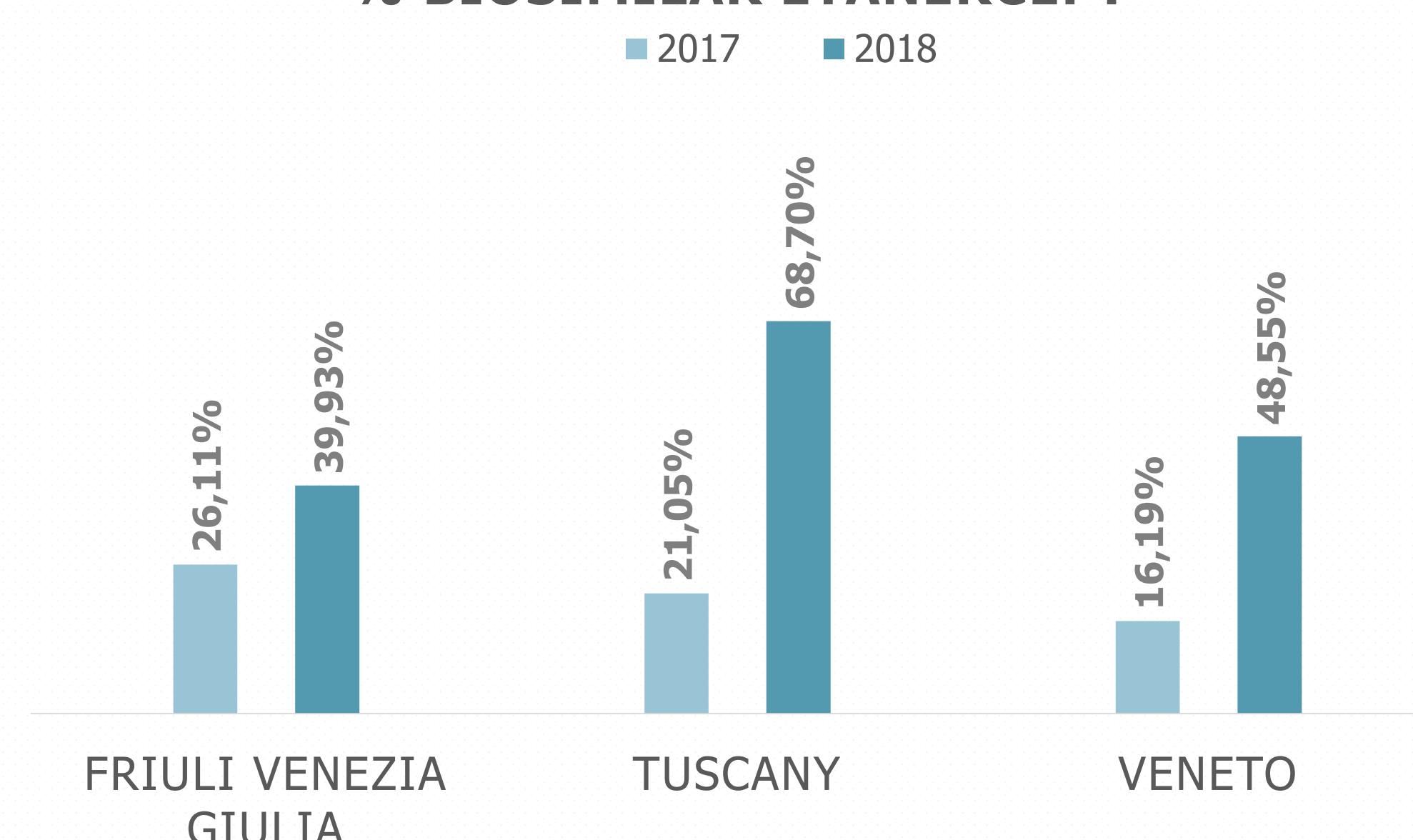
The panel of indicators on biosimilars, the definition and continuous revision of shared targets and the constant and systematic benchmarking fostered biosimilars penetration over the period 2017-2018 in Tuscany. The percentage of biosimilar molecule Etanercept, for instance, grew from 21,05% to 68,70%, the % Biosimilar Rituximab from 7,1% to 74,64%. The increase was either better or in line with that of the other Italian regions. The greater usage of biosimilars contributed to the reduction of the pharmaceutical expenditure of the Tuscan Region from € 1.157.044.094 in 2017 to €1.118.523.838 in 2018. However, both an intra and inter-regional avoidable unwarranted geographic variation was observed.

### % BIOSIMILAR RITUXIMAB



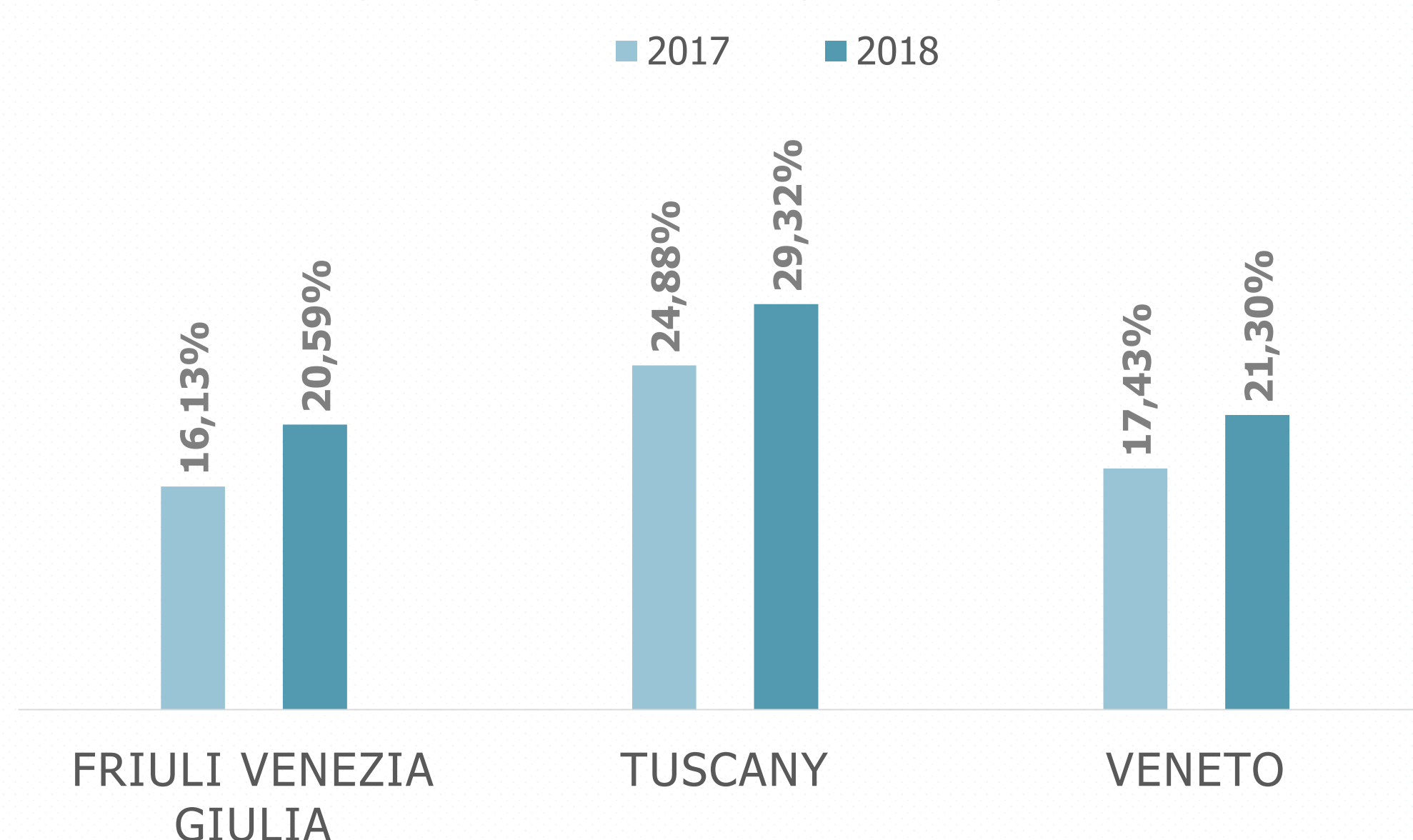
[The percentage of biosimilar Rituximab was calculated as milligrams of biosimilar Rituximab administered divided by total milligrams of Rituximab-based drugs administered]

### % BIOSIMILAR ETANERCEPT



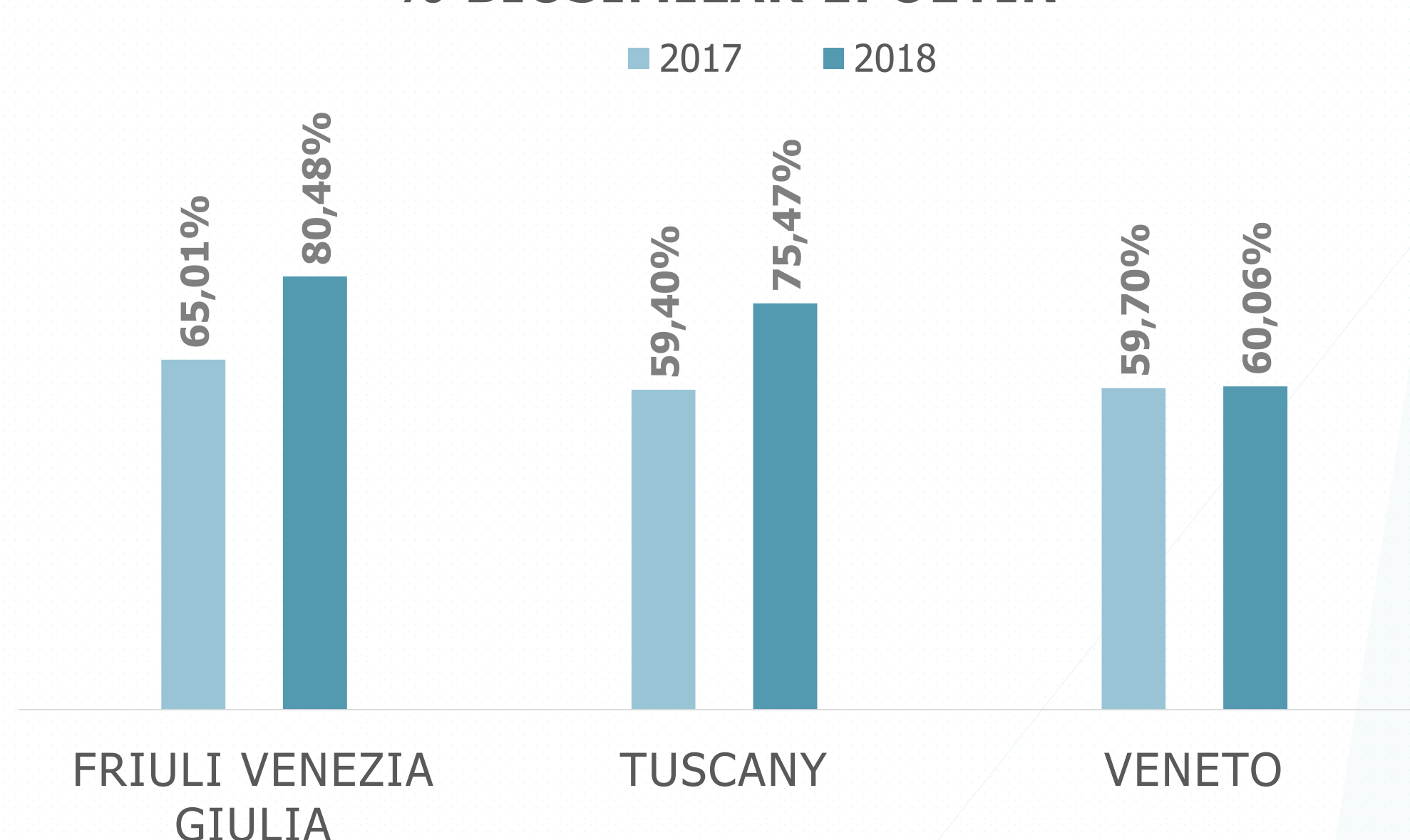
[The percentage of biosimilar Etanercept was calculated as number of patients treated with biosimilar Etanercept over total number of patients treated with Etanercept-based drugs]

### % BIOSIMILAR SOMATROPIN



[The percentage of biosimilar Somatropin was calculated as number of patients treated with biosimilar Somatropin over total number of patients treated with Somatropin-based drugs]

### % BIOSIMILAR EPOETIN



[The percentage of biosimilar Epoetin was calculated as number of patients treated with biosimilar Epoetin over total number of patients treated with Epoetin-based drugs]





# Medicines prices in Morocco

on average decreased  
since implementation of the  
2014 decree on medicines prices



Taking a closer look at the price set-up and evolution of margins:  
regulating prices should be closely linked to reviewing mark-up schemes and mechanisms

## Regulating medicine prices in Morocco - Effects of the medicine price decree 2014 on medicine prices

Bouchra Benslaoui<sup>1</sup>, Mohammed Wadie Zerhouni<sup>1</sup>, Anas Chikhaoui<sup>1</sup>, Fatima Zahra Ben Fouila<sup>2</sup>, Katharina Habimana<sup>3\*</sup>, Hafid Hachri<sup>4</sup>, Maryam Bigdeli<sup>4</sup>, Sabine Vogler<sup>3</sup>, Jamal Taoufik<sup>1</sup>

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<sup>2</sup> General Secretary, Ministry of Health, Rabat, Morocco

<sup>3</sup> WHO Collaborating Centre for Pharmaceutical Pricing and Reimbursement Policies, Austrian National Public Health Institute (Gesundheit Österreich GmbH), Vienna, Austria. \*corresponding author

<sup>4</sup> WHO Country Office Morocco, Rabat, Morocco

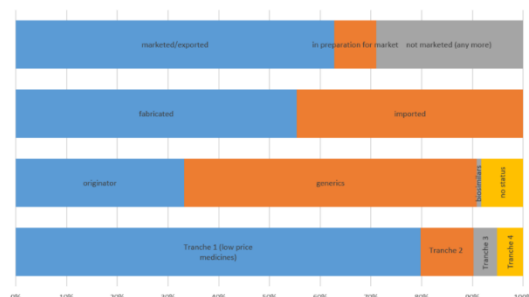
**Dataset:** 7,000 + medicines on Moroccan market

**Price data:** 2014-2019 for

- public prices
- pharmacy retail prices
- wholesale prices
- ex-factory prices

→ data availability before and after implementation of decree

Figure: Composition of data set (Source: DMP, prepared by authors)



**The 2009 Parliamentary Commission Report on medicines prices considered the Moroccan medicines prices too high compared to other countries.**

2013  
review of medicines price regulation in Morocco

2014  
implementation of decree  
for new provisions related to  
EPR, generic price link and  
changes in margins

2019  
evaluation of effects of medicines price decree

	TRANCHE DE PFHT EN DH	MARGE OFFICINE	MARGE GROSSISTE	FORFAIT OFFICINE EN DH	FORFAIT GROSSISTE EN DH
1	PFHT ≤ 166	57 %	11 %	-	-
2	166 < PFHT ≤ 588	47 %	11 %	-	-
3	588 < PFHT ≤ 1766	-	2 %	300	-
4	PFHT > 1766	-	2 %	400	-

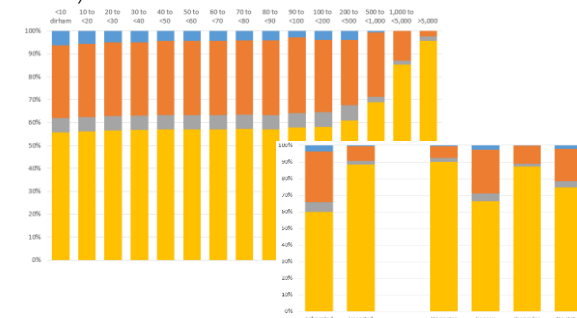
Full study will also contain qualitative  
analysis on stakeholders' views

## Selected findings

### Current medicines prices in Morocco

- currently 3,937 medicines commercialised/exported
- more than 600 medicines in price category of 10 to 20 dirham (0.94 to 1.87 Euro)
- price composition differs between price categories and status

Figure: Price composition by price level (Source: DMP, prepared by authors)



### Evolution of medicines prices in Morocco since implementation of Decree

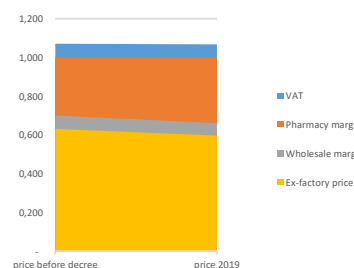
- price data available before and after implementation of decree for 4, 917 medicines (including non-marketed)
- for (still) commercialised medicines prices and margins decreased, on average, for all price levels after implementation of the Decree, wholesale margins decreased, pharmacy margins increased on average

Table: Evolution of price and margin for commercialised medicines (source: DMP, prepared by authors)

	mean	minimum	1st quartile	median	3rd quartile	maximum
Public price	-6,9%	-78,6%	-6,5%	0,0%	0,0%	142,7%
VAT	-3,0%	-73,2%	-0,1%	0,0%	0,0%	142,7%
Pharmacy retail price	-6,9%	-78,6%	-6,5%	0,0%	0,0%	142,7%
Pharmacy margin	2,9%	-94,4%	-1,6%	13,1%	13,1%	173,0%
Pharmacy purchase price	-11,1%	-79,8%	-8,6%	-5,6%	-5,6%	129,8%
Wholesale margin	-14,5%	-92,1%	-11,7%	-6,5%	-6,5%	127,7%
Ex-factory price	-10,7%	-79,8%	-6,6%	-5,5%	-5,5%	130,0%

- pharmacy margins reduced rather for high prices medicines; for lower priced medicines pharmacy margins may have increased, as illustrated in following example

Figure: Paracetamol 500 mg, example evolution of price set-up after implementation of decree (Source: DMP, prepared by authors)

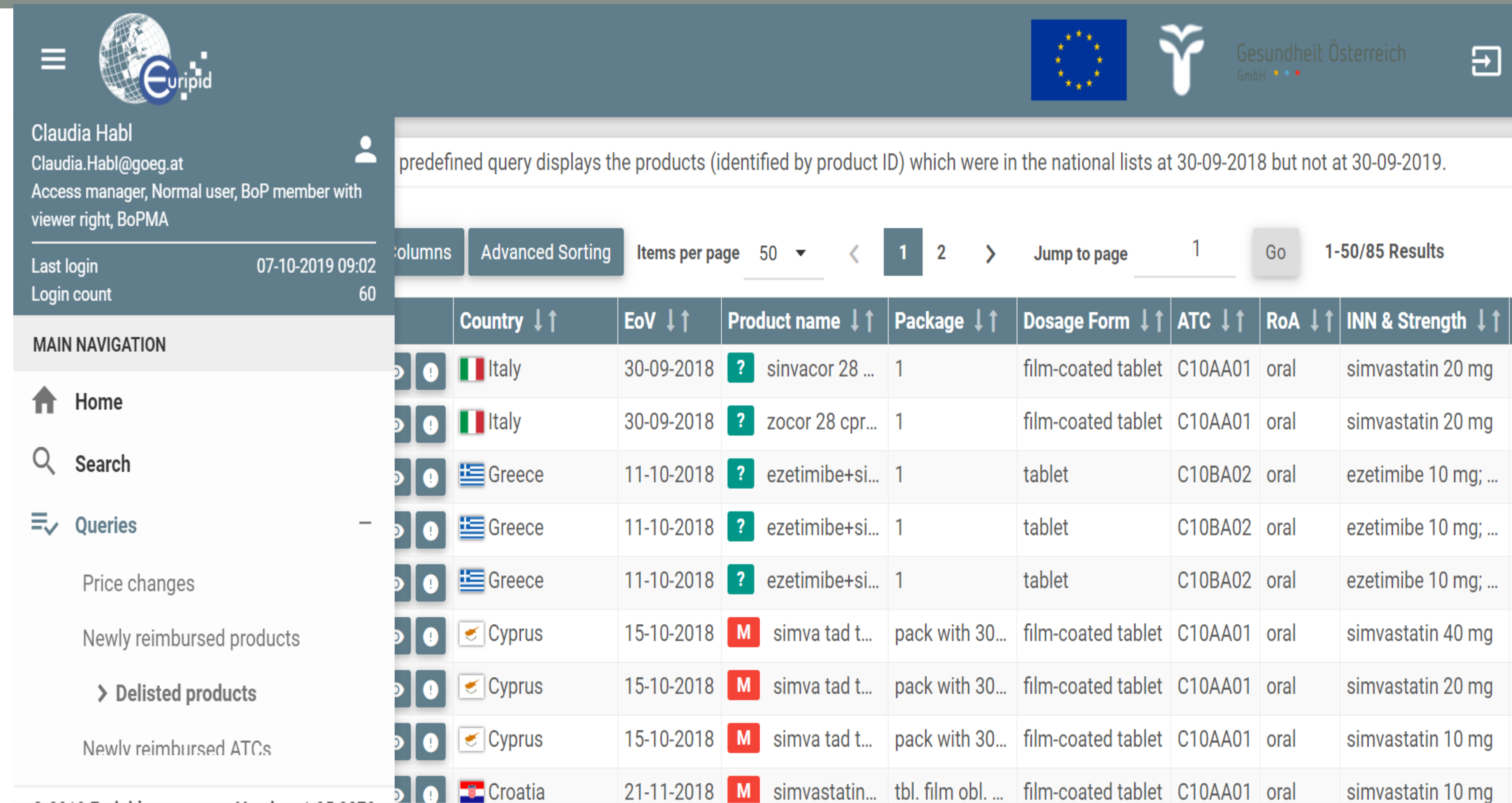




# How the Euripid Collaboration contributes to the affordability of medicines in Europe

Claudia Hahl, Gergely Nemeth and Peter Schneider on behalf of the Executive Committee of the Euripid Board of Participants

- EURIPID ([www.euripid.eu](http://www.euripid.eu)) is a voluntary collaboration between European countries to run a database with information on national prices of pharmaceuticals in a standardised format.
- Prices of publicly funded medicines are made more transparent via a reliable 24-hour-online database.
- Access only for registered users, currently from 26 countries + EC.



The screenshot shows the Euripid website interface. On the left, a user profile for Claudia Hahl is visible, including her email (Claudia.Hahl@goeg.at) and login details. The main area displays a table of pharmaceutical products. The table has columns for Country, EoV, Product name, Package, Dosage Form, ATC, RoA, and INN & Strength. The data shows products from Italy, Greece, Cyprus, and Croatia, with details on their prices, dosages, and forms.

Country	EoV	Product name	Package	Dosage Form	ATC	RoA	INN & Strength
Italy	30-09-2018	sinvacor 28 ...	1	film-coated tablet	C10AA01	oral	simvastatin 20 mg
Italy	30-09-2018	zocor 28 cpr...	1	film-coated tablet	C10AA01	oral	simvastatin 20 mg
Greece	11-10-2018	ezetimibe+si...	1	tablet	C10BA02	oral	ezetimibe 10 mg; ...
Greece	11-10-2018	ezetimibe+si...	1	tablet	C10BA02	oral	ezetimibe 10 mg; ...
Greece	11-10-2018	ezetimibe+si...	1	tablet	C10BA02	oral	ezetimibe 10 mg; ...
Cyprus	15-10-2018	simva tad t...	pack with 30...	film-coated tablet	C10AA01	oral	simvastatin 40 mg
Cyprus	15-10-2018	simva tad t...	pack with 30...	film-coated tablet	C10AA01	oral	simvastatin 20 mg
Cyprus	15-10-2018	simva tad t...	pack with 30...	film-coated tablet	C10AA01	oral	simvastatin 10 mg
Croatia	21-11-2018	simvastatin...	tbl. film obl. ...	film-coated tablet	C10AA01	oral	simvastatin 10 mg

## Guiding Principles for External Price Referencing (ERP) of Medicinal Products

1. ERP is an important policy tool that should be used in a mix with other instruments and not as stand-alone policy tool.
2. ERP should take place on single product basis rather than by indices.
3. The aim of the national pharma policy should determine the selection of reference countries.
4. Evidence has shown that ERP is most effective when applied to medicines without generic or therapeutic competition.
5. Comparison of prices of medicines should be done on the 1<sup>st</sup> price (type) in the distribution chain.
6. Authorities should apply clear and transparent procedures to determine which medicines are considered as comparable.
7. The pricing formula applied should reflect the national objective of ERP.
8. ERP procedures should be performed with the highest accuracy and completeness of data sources.
9. If price information is adjusted to national requirements, it should be done in a transparent and sustainable manner.
10. ERP activities need careful planning → consider it as a policy tool for price revisions and monitoring.
11. The procedures and price inputs to ERP should be as transparent as possible, to ensure predictability and effectiveness.
12. Policy-makers should consider strengthening their cooperation, in particular through the contribution and benefits of existing policies.

## Conclusions and Lessons Learned

- The twelve principles are an important step towards a more **balanced use of ERP policy** and thus a higher acceptance in Europe.
- The **Euripid database** is aiding countries to perform price comparisons for ERP or price monitoring in a **standardised format**.
- A **stakeholder dialogue platform** was founded in April 2019 to allow a continuous information exchange in the area of pricing of medicines in Europe.
- Efforts are made to improve affordability of medicines by better price transparency (e.g., adding information on MEA + volumes → see the recent **WHO Transparency Resolution** that urges countries to take appropriate measures.



Source: [https://jasmin.goeg.at/432/1/EURIPID\\_GuidanceDocument\\_V8.1\\_310718.pdf](https://jasmin.goeg.at/432/1/EURIPID_GuidanceDocument_V8.1_310718.pdf)



# National reimbursement policies need to reflect public preferences by engaging the public through deliberative processes.

## Integrating public preferences into national reimbursement decisions: A descriptive comparison of approaches in Belgium and New Zealand

 Christine Leopold<sup>1</sup>, Christine Y. Lu<sup>1</sup>, Anita K. Wagner<sup>1</sup>  
<sup>1</sup> Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, MA, USA.

### INTRODUCTION

1. Increasing pressures to make transparent and sustainable coverage decisions.
2. Need for public engagement in coverage decisions.

### OBJECTIVES

Aim is to explore how Belgium and New Zealand used deliberative processes to engage the public to change their public reimbursement system and to identify lessons learned from these countries' approaches.

### METHODS

1. Review of key country documents
2. Semi-structured interviews of 5 key stakeholders
3. Qualitative content analysis

### LESSONS LEARNED

1. Need for political commitment to initiate change.
2. Need for broad involvement of all stakeholders.
3. Need for commitment of all to engage in a long-term process.

Organization leading the process	
<b>Belgium</b> National payer organization RIZIV/INAMI & 2 independent research institutions (KBF, KCE)	<b>New Zealand</b> National payer organization PHARMAC
Situation analysis	
<b>Belgium - 2010</b> - Report on "Drug reimbursement system: international comparison and policy recommendations" (KCE report 147C)	<b>New Zealand - 2012</b> - Group discussions at PHARMAC's public forum to review OPP
Type and structure of stakeholder engagement	
<b>Belgium</b> - 2012 - Formation of steering committee - 2014 - Formation of new Reimbursement Commission - Workshops with experts - Survey among the population	<b>New Zealand</b> - Various public consultations - Written feedback (including from consumers, Maori community, pharmaceutical industry, clinicians, professional organizations & members of the public and state sector agencies)
Identification of relevant criteria / methods & collection of data	
<b>Belgium – 2012 to 2014</b> - EU workshops on "Justice & solidarity in priority setting" (KBF 2013) - Delphi panel on "Models for citizen and patient involvement in health care policy" (KCE 195C)	<b>New Zealand – 2013</b> - 20 publications by leading academics on issue of access to and affordability of health care services - PHARMAC published information material
Deliberation and mode of outreach	
<b>Belgium – 2014</b> - Discrete choice survey "Incorporating societal preferences in reimbursement decisions" (online with 4449 participants, KCE 234) - Citizen-lab (f2f on 3 weekends with 32 participants) - Citizen-dialogue in 10 regions organized by payer (f2f with around 400 participants)	<b>New Zealand – 2013 to 2014</b> - 2013 PHARMAC's senior leadership lead 12 community forums (in churches, town halls etc.) - 2014 f2f stakeholder event - 2014 written comments with wide-ranging stakeholders (n= 49)

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# Predictability and transparency were key for ensuring medicine price stability: based on a cross-government structure, governance and enforcement mechanisms, a technical body to support decision making, contributing to economic growth and access.



## 18 years of economic regulation of medicines in Brazil: outcomes, challenges and lessons learnt

Adriana M Ivama-Brummell<sup>1\*</sup>, Daniella Pingret <sup>1</sup>, Rosiene R de Andrade<sup>1</sup>, J Ricardo Santana<sup>1</sup>

<sup>1</sup> Medicines’ Market Regulation Chamber Executive Secretariat (SCMED)/Brazilian Health Regulatory Agency (Anvisa), Brasília, Brazil; E-mail: [adriana.ivama@anvisa.gov.br](mailto:adriana.ivama@anvisa.gov.br)

### INTRO

- The current health and economic medicines regulatory framework emerged from a deep crisis in the Brazilian pharmaceutical sector with falsified and substandard medicines, shortages, very high prices, among other practices.

### OBJECTIVES

To review the implementation of the economic regulatory framework for medicines in Brazil and the adopted regulatory policy options based on WHO recommendations, describing its outcomes, challenges and perspectives

### METHODS

- Policy analysis combining descriptive with qualitative analysis;
- Data review from official databanks: such as the Medicines’ Market Monitoring System (SAMMED) and the national public procurement system (Compras-net).
- Region covered: Brazil (PAHO/WHO region).

### RESULTS

- The national medicines’ policies and economic regulatory framework established in 2001 following WHO recommendations (Table 1) provided for a stable structure, governance and enforcement mechanisms, with a technical body to support decision making, leading to medicines’ price stability, arising mostly below inflation levels (Figure 1).

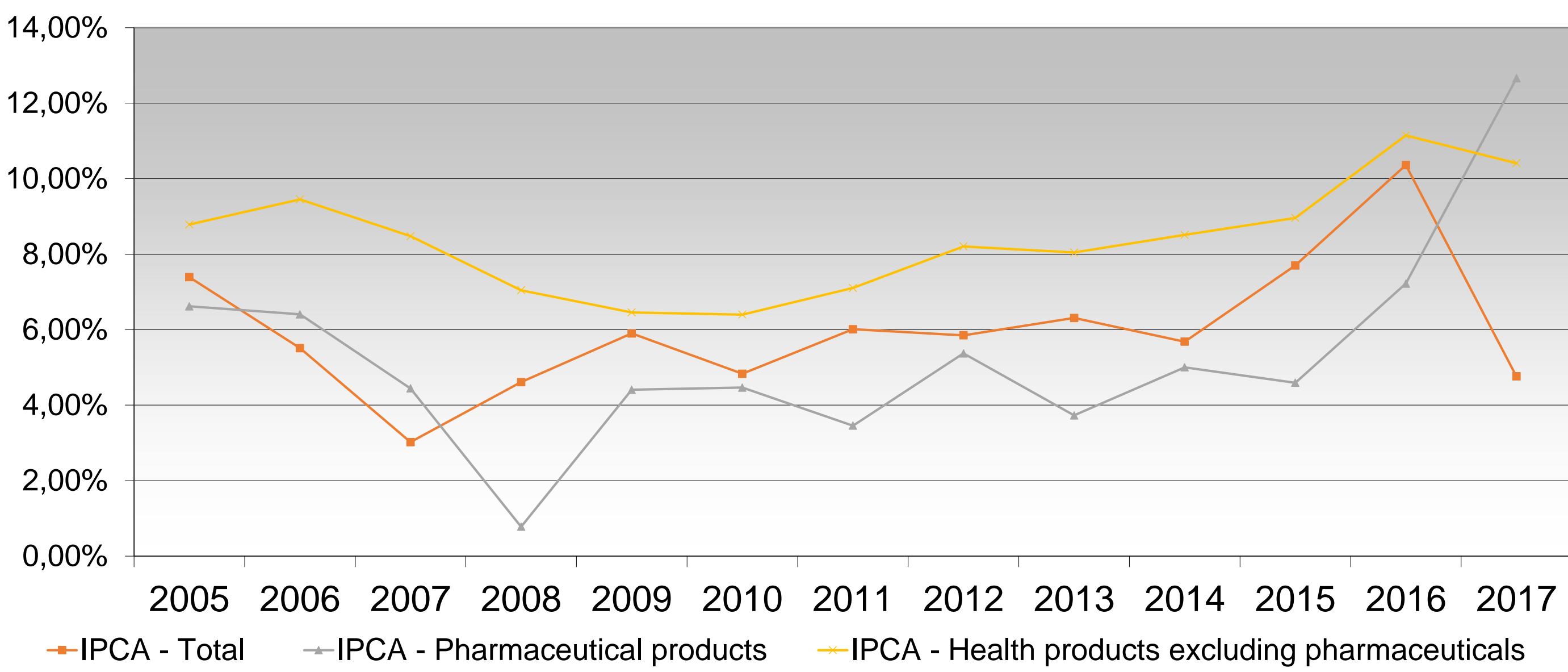


Figure 1. IPCA (Broad Consumer's Prices National Index) and average authorised adjustment of the medicines' market (2005 - 2017).

Source: SCMED

- There was an increase of new medicines in the Brazilian market: from 2011 to 2017: 230 new medicines entered the Brazilian market. 201 (87%) of them from transnational and 29 (13%) from national companies, with 25 different therapeutic classes.
- In 2017, the revenue of the Brazilian pharmaceutical market was USD 21 billion with 4.4 billion units commercialised (1.4 billion units of generic medicines, 32.4%).
- In 2018, the mandatory discount for public procurement was 20.16% of the maximum prices, leading to important savings.

### CONCLUSIONS AND LESSONS LEARNT

- The intersectoral governance mechanism of CMED and the regulatory system allowed for it be consolidated as a State policy, being able to continue through different governments.
- The pharmaceutical sector continued growing, even during austerity periods.
- The challenges include the need of improving the regulatory framework, appraisal process and transparency and find alternatives for high priced medicines with preliminary or poor-quality evidence and without ERP.

Table 1. Summary of the principles recommended by WHO implemented in Brazil from 2001-2019

WHO principles	Implemented policy intervention/outcome in Brazil*
Use a combination of different pharmaceutical pricing policies	Different legal instruments for pharmaceutical pricing policies and regulation, medicines production and innovation, incorporation and procurement established by different laws and policies.
Transparent pricing policies, processes, and decisions	Rules, criteria for pricing and the decisions taken are standardised and transparent, including authorised prices and public procurement prices public available (electronic systems for price application; procurement prices).
Appropriate legislative framework, governance and administrative structures, supported by technical capacity, and regularly reviewed, monitored and evaluated	The Law 10.742/2003 set the basis for medicine price regulation and established a governance and administrative structure – the Medicines’ Market Regulatory Chamber (CMED) with representatives from the Ministry of Health (President), the Presidency’s Office (Casa Civil), the Ministry of Economy and Ministry of Justice and Public Security. The decision-making levels are: <ul style="list-style-type: none"><li>the Ministerial Council, the Executive;</li><li>Technical Committee (CTE) and</li><li>Executive Secretariat (SCMED), at the Brazilian Health Regulatory Agency (Anvisa), a technical body for supporting the decision making, implementing its decisions and monitoring the pharmaceutical market.</li></ul>
Combination of pharmaceutical policies	The national medicines policy (1998), pharmaceutical services policy (2004) and science and technology in health policy (2005), among others, address both supply and demand issues. These policies were formally approved and implemented.
Effective implementation of regulation of pharmaceutical prices and ensure compliance	Enforcement mechanisms and monitoring system with enforcement power in place to ensure compliance of the price regulation. Annual adjustment are authorised (not mandatory) based on productivity factor, intra-sectoral factor and inter-sectoral factor (with calculating parameters defined and publicly available, including the Broad Consumer's Prices National Index (IPCA) (Law 10.742/2003 and additional regulations). Price not reviewed.
Policies to promote the use of quality assured generic medicines to increase access and affordability.	Generic medicines’ policy and legal framework (Law 9.787/1999) with regulations from Anvisa setting requirements for quality, safety, efficacy, prescribing by the international non-proprietary name (INN) and generic substitution and pricing rules (Res 02/2004) fully implemented.
Countries’ collaboration/exchange of information	Brazil is a member of networks of the America’s Regional Initiative of competent authorities related to price policies and regulation and the network of Health Technology Assessment of Americas (Redetsa), both supported by PAHO/WHO.



Price regulation, the mandatory minimum discount and a maximum government procurement price (PMVG) have led to great savings, helping to increase the access to medicines. They allowed the procurement of more than twice the volume for 2,3 times the number of patients in 2018, compared to the previous year.



## Case study of the judicialisation of eculizumab (Soliris®): challenges in the price regulation and the impact of establishment of the maximum government price in Brazil

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### INTRO

- In Brazil, access to health, including the access to medicines is a Constitutional right;
- Due to limited budgets, there is “judicialisation” (court cases) to ensure access to medicines in the Unified Health System (SUS);

### OBJECTIVES

The objective of this study was to describe and review how the economic regulation has contributed to promote access to medicines for very high-priced medicines in Brazil.

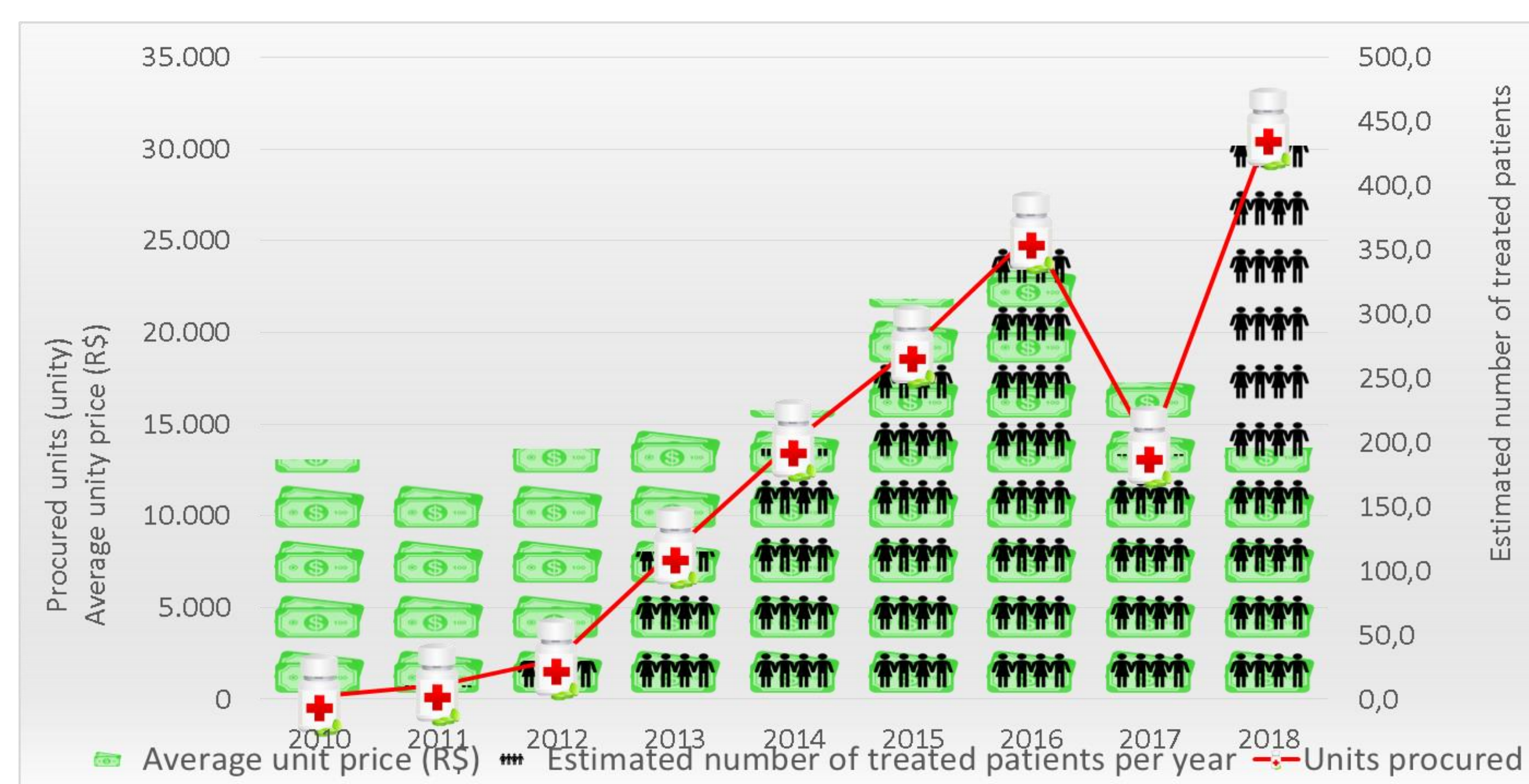
### METHODS

- Policy analysis combining a descriptive study with data review from the Medicines' Market Monitoring System (SAMMED) and the national public procurement system (Compras-net) regarding the procurement of eculizumab (Soliris) from 2010 to 2018, reviewing key results.
- Region covered: National study in Brazil (PAHO/WHO region).

### RESULTS

- In 2016, eculizumab (Soliris®), for treatment of paroxysmal nocturnal haemoglobinuria (PNH), a rare disease, costed USD 187 million (R\$ 620 million) to the SUS (average unit price: USD 8.347,82, R\$ 27,614.60), purchased due to court cases, before marketing authorisation and its incorporation to the health system.
- In 2017, when the eculizumab became regulated by CMED, it had a CAP discount of 19,28% and CMED established the PMVG of USD 3.710,00 (R\$ 12,274.83).

- Due to this price difference, in 2018, MoH purchased more than twice the volume (31,056 units for 431 patients) compared to 2017 (13,721 units for 190 patients), based on the recommended daily doses for adults in the main indication (figure 1).



\* The average procurement price was calculated based on the different procurement processes through each year and number of units and the estimated number of treated patients per year was calculated based on the adults' recommended daily doses for paroxysmal nocturnal haemoglobinuria (PNH)

Figure 1. Number of units, average unit price of eculizumab (Soliris®) procured by the Brazilian Ministry of Health and the estimated number of treated patients from 2010-2018.

### CONCLUSIONS AND LESSONS LEARNED

- External Reference Pricing (ERP) is still a very useful tool for pricing. Therefore, price transparency and cooperation with information sharing among countries is important.
- Despite great savings and increased access to medicines, there are still challenges for the health system in providing very high-priced medicines, with few or no external reference prices.
- The legal provision for setting a provisional maximum price and PMVG “ex officio” with administrative process and penalties for commercialisation before approval can contribute to tackling very high prices.

### Price Regulation

- The Law 10.742/2003 sets the basis for medicines prices regulation and established a governance and administrative structure – the Medicines' Market Regulatory Chamber (CMED) with representatives from the Ministry of Health (President), the Presidency's Office (Casa Civil), the Ministry of Economy and Ministry of Justice and Public Security.
- The Medicines' Market Regulatory Chamber (CMED) regulates medicines' prices (price cap) since 2003, based on Health Technology Assessment, External Reference Pricing (ERP) and Internal Reference Pricing (IRP).
- In 2006, CMED established the Price Acquisition Coefficient (CAP), a mandatory minimum discount with a maximum government procurement price (PMVG) to a positive list of medicines.
- The Resolution CMED no. 2/2018 established that it is an infringement to offer a medicine without an authorised price by CMED and that CMED will provisionally set the maximum price allowed (*ex officio*).



# High-cost specialty therapies dominate the new medicine landscape

## Insight into the market for new medicines

With rising numbers of new drug market approvals and increasingly specialized therapies in the pipeline, new medicines represent a growing source of cost pressure for payers in Canadian and global markets. In 2018, nearly 6,000 new medicines were in clinical evaluation and pre-registration with the US Food and Drug Administration (FDA), representing 87% of the total pipeline. Over 700 new medicines were in the late stages of development, and a total of 51 medicines were approved internationally in 2018. Of these 51, more than half had an orphan designation, while almost a third were for the treatment of cancer.

Using data from the IQVIA MIDAS® Database and the GlobalData Healthcare Database, this study features pipeline candidates in Phase III clinical trials or pre-registration with the FDA, and analyzes the market entry dynamics of new medicines approved in Canada and internationally in 2018. Pipeline medicines are selected for their potential impact on future clinical practice and/or drug spending. Newly approved medicines are identified based on the date of first-time market approval by the FDA, the European Medicines Agency (EMA), and/or Health Canada.

### 1. A dominant share of new medicines in development are indicated to treat cancer

Many new oncology medicines in the pipeline and on the market have come with orphan designations. This may be the result of the introduction of precision technology, such as biomarkers, which has allowed cancer therapies to become more targeted and disease-specific.

- Oncology treatments dominated the 2018 pipeline, accounting for roughly one third of medicines in all phases of clinical evaluation.
- More than 300 orphan-designated cancer treatments are currently in research and development with over 200 companies.
- Other prominent therapeutic areas included treatments for infectious diseases such as HIV and pneumonia (12% of medicines) and medicines for nervous system diseases such as Alzheimer's disease and depression (11% of medicines).

### 2. Medicines for rare diseases continue to represent a significant share of the pipeline

Recent innovation in pharmaceutical technology has shifted the new medicine landscape toward specialty therapies, such as medicines for rare diseases and cancer treatments that target specific genetic deficiencies.

- Orphan medicines accounted for 16% of the total pipeline, and 29% of Phase III clinical trials in 2018.
- This share increased to 40% for the oncology medicines undergoing Phase III clinical trials and pre-registration.
- Of the medicines that reached approval in Canada by Q4-2018, more than half (59%) had received an orphan designation from either the FDA or the EMA.

### 3. A greater than average number of new medicines were approved in 2017 and 2018, including an increasing share of specialty therapies

In 2018, 51 medicines received first-time approval through the FDA, the EMA, and/or Health Canada. By comparison, 31 new medicines were approved in 2016, and the annual average between 2009 and 2015 was 36.

- Over half (30) of the 2018 new medicines received an orphan designation from the FDA or EMA, explaining the rising share observed over recent years.
- Almost one third (15) of new medicines were approved for cancer indications, seven of which were orphan-designated oncology treatments.

### 4. Sales of 2018 new medicines were concentrated in four therapeutic areas, with one HIV treatment making up over half of the total revenues

Although new medicines launched in Canada and the PMPRB7\* in 2018 covered a wide range of therapeutic areas, their sales were highly concentrated.

- 10 of the 51 medicines, representing the top four therapeutic classes, accounted for over 90% of all 2018 new medicine sales in Canada and the PMPRB7 by Q4-2018.
- One new treatment achieved blockbuster status within less than a year of market entry: Biktarvy, an orphan-designated medicine indicated to treat HIV, was approved in the US in February 2018, and Europe and Canada the following July.
- Despite demonstrating slight or no improvement over existing therapies, as assessed by the PMPRB's Human Drug Advisory Panel, Biktarvy accounted for 52.5% of the total sales for all new medicines in Canada and the PMPRB7 by Q4-2018.

Figure 1: Therapeutic distribution of pipeline medicines by phase of development, 2018

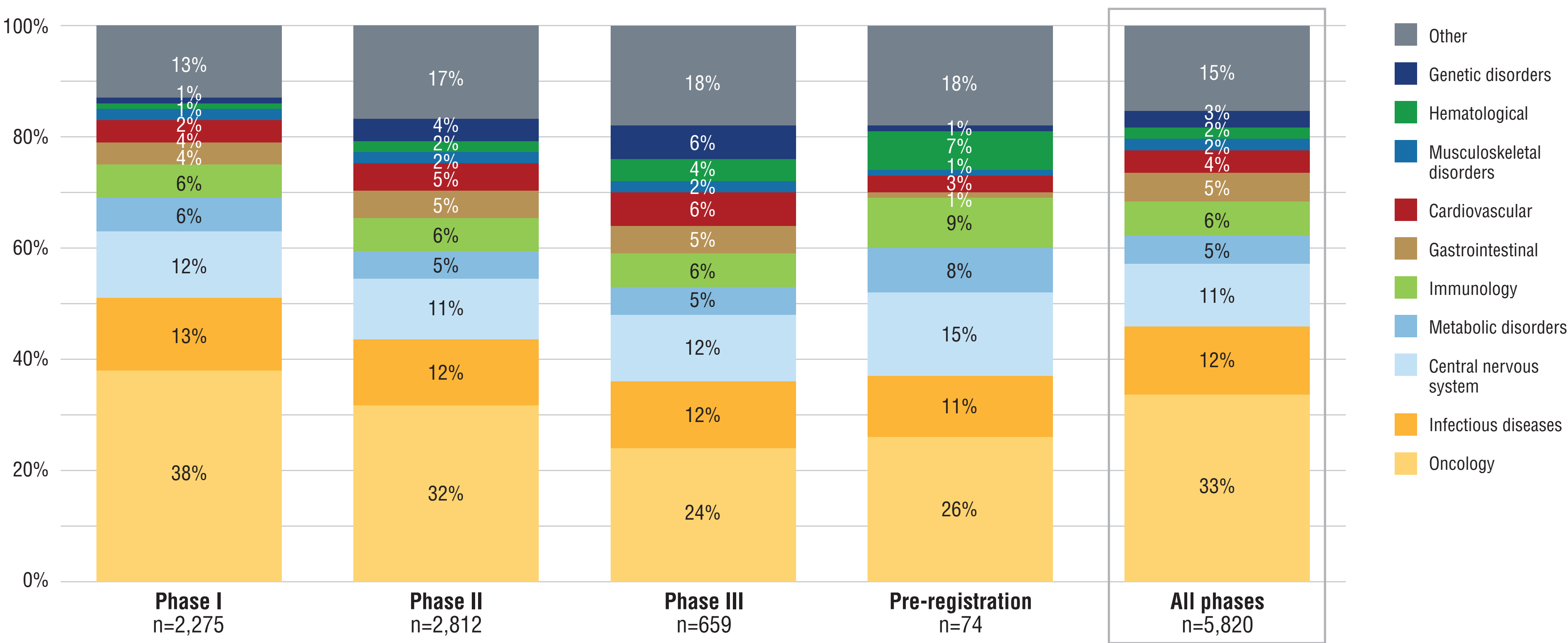


Figure 2: Orphan designations for new medicines by phase of clinical evaluation and approval, 2018

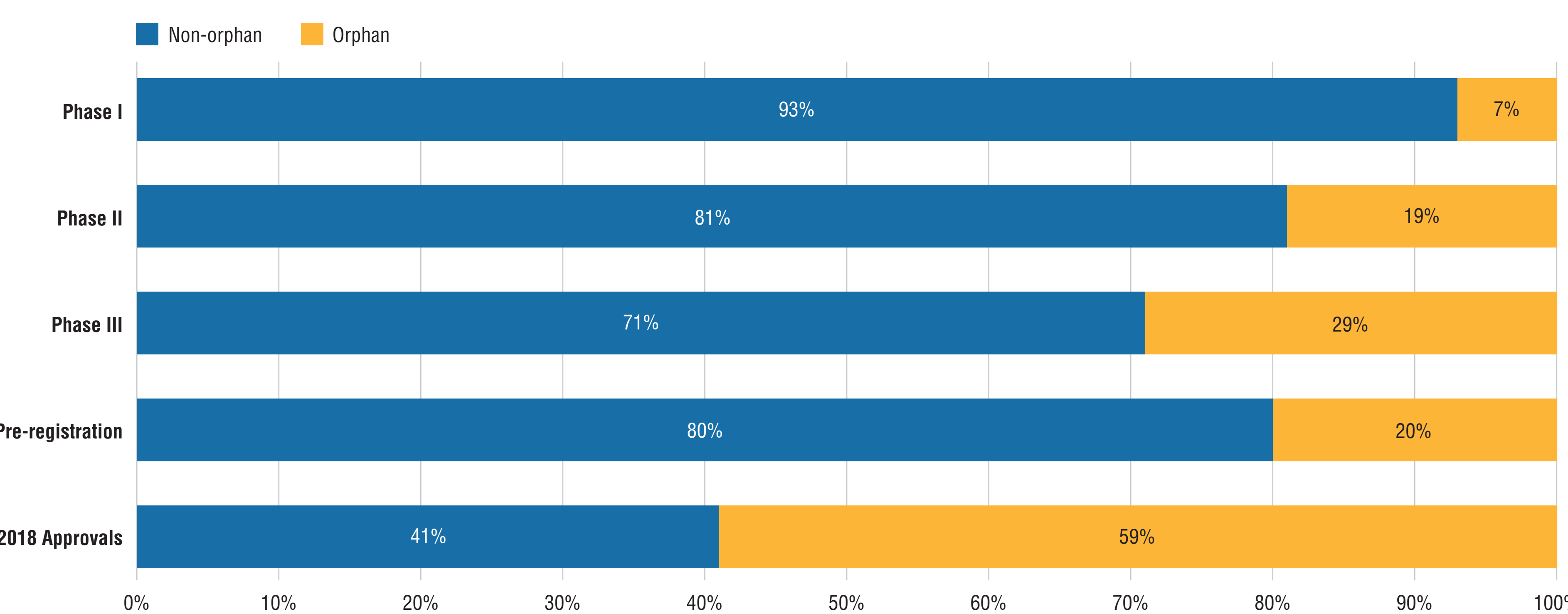


Figure 3: New medicines approved by the FDA, the EMA, and/or Health Canada, 2016 to 2018

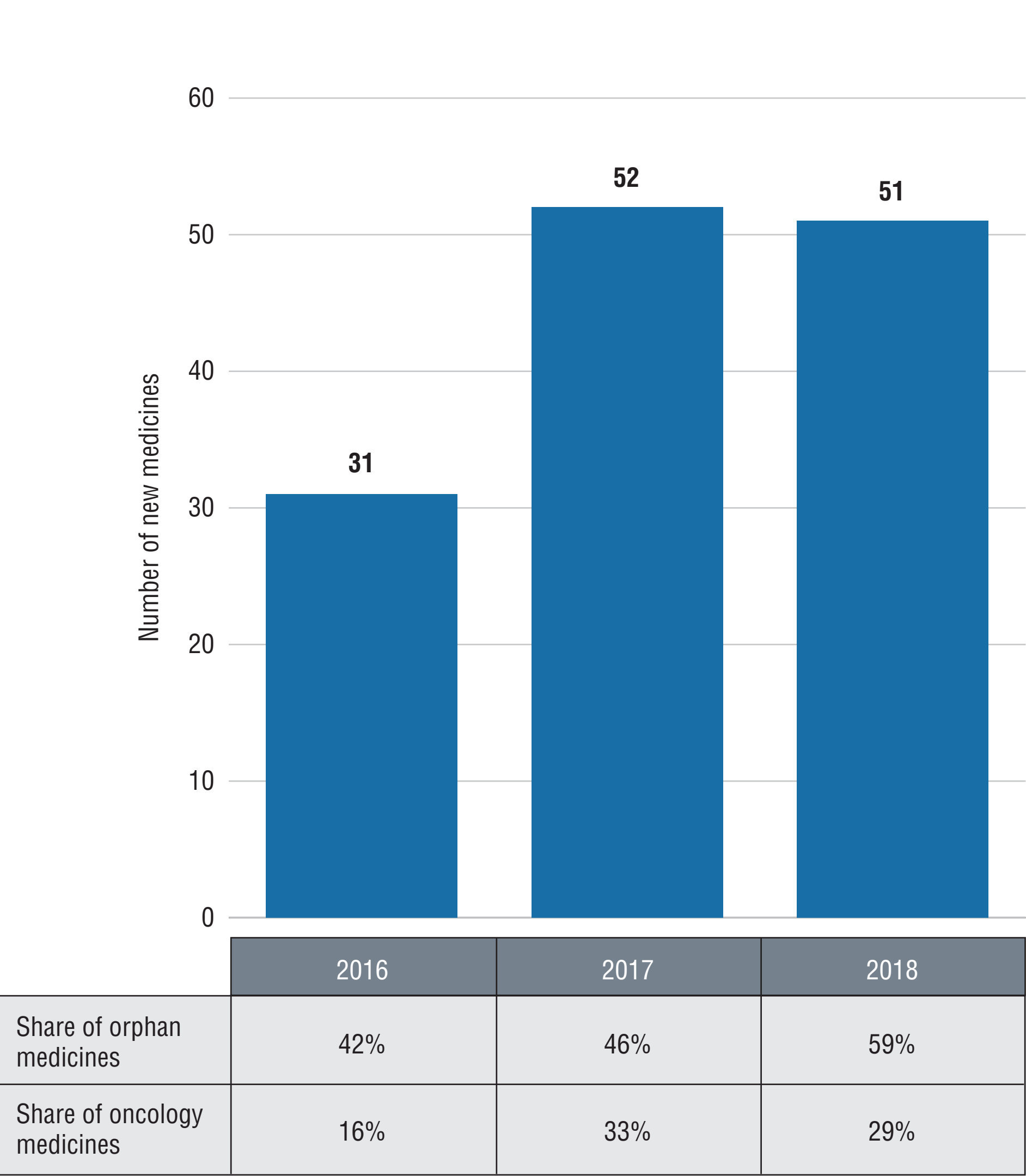
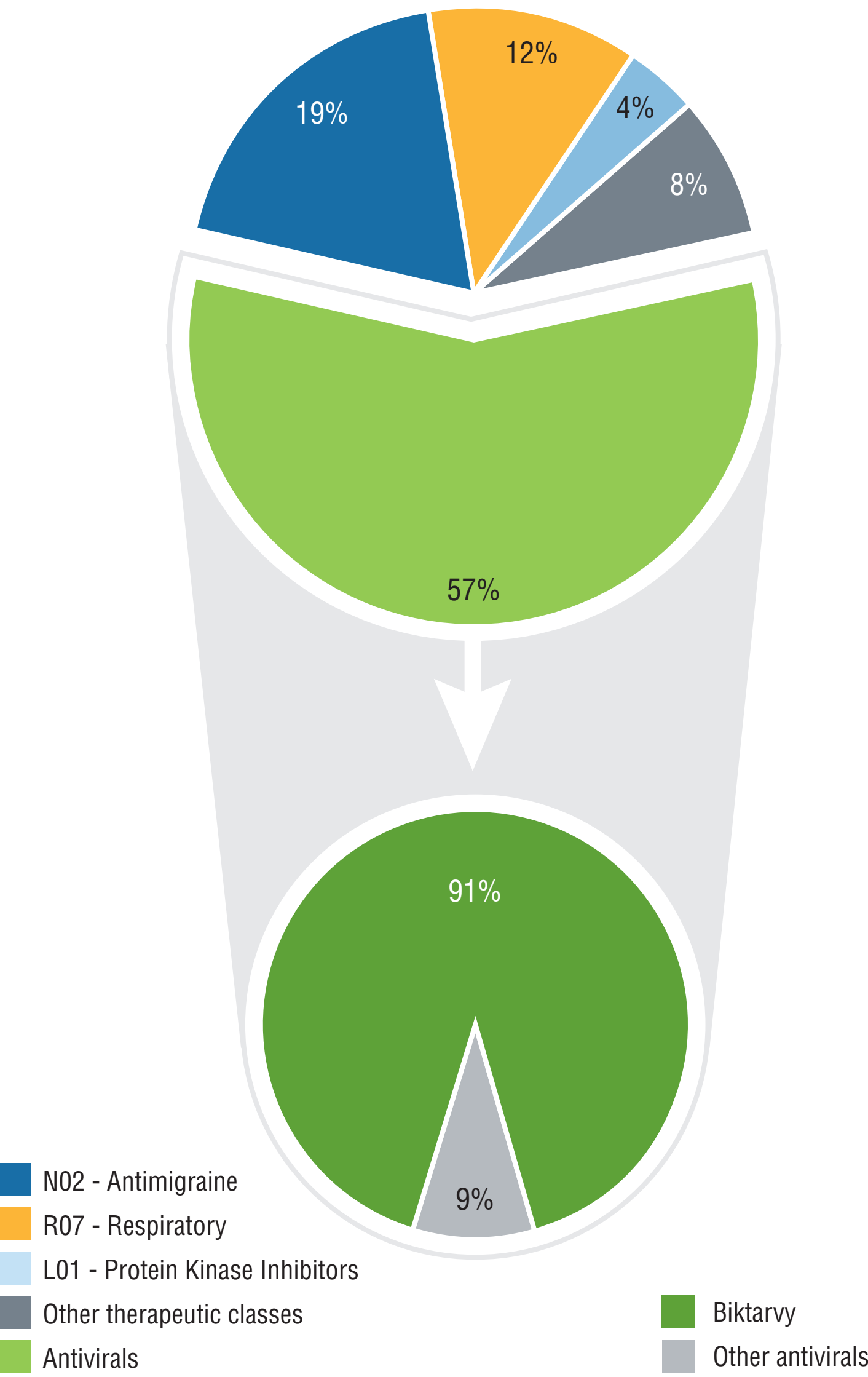


Figure 4: Distribution of new medicines by therapeutic class, Canada and the PMPRB7, Q4-2018



\* France, Germany, Italy, Sweden, Switzerland, the United Kingdom, and the United States.

Data source: IQVIA MIDAS® Database (all rights reserved), 2016 to 2018; GlobalData Healthcare database (accessed July 2018).

Limitation: Canadian and international sales and list prices available in the IQVIA MIDAS® Database are estimated manufacturer factory-gate list prices and do not reflect off-invoice price rebates and allowances, managed entry agreements, or patient access schemes.

Disclaimer: Although this information is based in part on data obtained under license from IQVIA's MIDAS® Database and the GlobalData Healthcare database, the statements, findings, conclusions, views, and opinions expressed in this study are exclusively those of the PMPRB and are not attributable to IQVIA or GlobalData.

This analysis was undertaken by the NPDUIS research initiative, which operates independently of the regulatory activities of the PMPRB.



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Conseil d'examen  
du prix des médicaments  
brevetés

Patented Medicine Prices Review Board  
333 Laurier Avenue West, Suite 1400  
Ottawa, ON K1P 1C1  
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Canada



# The PMPRB now has the tools and information needed to **meaningfully protect Canadian consumers** from excessive prices today and into the future

## Patented Medicine Prices Review Board Framework Modernization

Canada has recently amended its Patented Medicines Regulations, bringing significant enhancements to its regulatory price regime, and providing the Patented Medicine Prices Review Board (PMPRB) with the tools and information it needs to protect Canadians from excessive medicine prices today and into the future.

As the regulator responsible for giving effect to the amendments on July 1, 2020, the PMPRB is consulting its stakeholders and the public on new pricing Guidelines, to ensure they are fair, functionally sound, and rationally connected to the nature and scope of the regulatory changes.

.....

The current regulatory pricing framework provides the PMPRB with dated tools to fulfill its consumer protection mandate. In essence, it simply relies on internal and external price referencing that includes premium priced comparator countries, most notably the United States. The framework also regulates prices at list-price level, which are not reflective of confidential rebates negotiated by manufacturers and payers. In today's environment, medicines are often priced for value, a factor not in the PMPRB toolbox, and some may create affordability challenges for consumers given their large market size. The existing framework poses a very real threat to the sustainability of the pharmaceutical system in Canada, which was the impetus for the regulatory framework modernization for patented medicine price.

The regulatory amendments update the PMPRB's framework to a risk-based approach that includes (1) a new schedule of countries, (2) additional price regulatory factors, and (3) patentee information reporting requirements, as described below.

### 1. An updated schedule of comparator countries

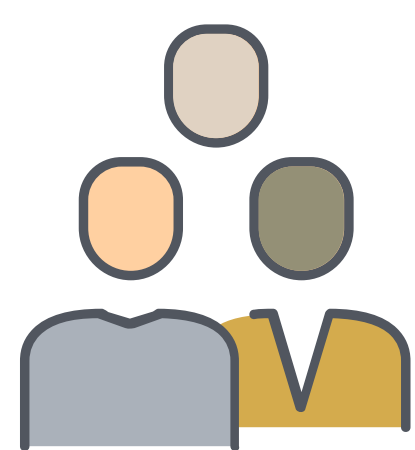
The new framework includes countries with similar consumer protection priorities, economic wealth, and marketed medicines as Canada. The basket of comparator countries now also includes Australia, Belgium, Japan, Netherlands, Norway, and Spain, while the premium priced countries, such as the United States and Switzerland, were removed from the list.

Previous comparator countries: PMPRB7	Foreign-to-Canadian price ratio*	New comparator countries: PMPRB11
France	0.76	France
Germany	0.97	Germany
Italy	0.85	Italy
United Kingdom	0.83	United Kingdom
Sweden	0.86	Sweden
Switzerland	1.06	Australia
		Belgium
		Japan
		Netherlands
United States	3.21	Norway
		Spain

\* Average foreign-to-Canadian price ratios are calculated based on patented medicines prices reported in IQVIA's MIDAS® Database. Note that Canadian and international prices available in MIDAS are estimated manufacturer factory-gate list prices and do not reflect off-invoice price rebates or managed entry agreements.  
Data source: PMPRB Annual Report, 2017.


### 2. Additional price regulatory factors

The new regulatory framework adds new factors that the PMPRB must consider when determining whether the price of a patented medicine is excessive, and now includes the medicine's value to and financial impact on consumers in the health system. The addition of the new factors allows the PMPRB to assess the economic impact of a patented medicine's price, enabling it to develop screening criteria for medicines that are likely to pose affordability challenges. The amendments bring Canada in line with other countries that are adopting newer methods of evaluating prices by looking at the cost of the medicine relative to its health benefits and the impact reimbursement has on overall health system expenditure.



#### Pharmacoeconomic value

A measure of how much a medicine costs for the health benefit it provides



#### Market size

Takes into account the impact of paying for the medicine for everyone who needs it

#### GDP and GDP per capita

These are indicators of the overall societal and individual wealth in Canada

### 3. Changes in reporting requirements

The new framework requires the actual price obtained by the patentee to be reported to the PMPRB, taking into account any adjustments. This includes reporting the confidential rebates and discounts that manufacturers negotiate in confidence with payers and do not disclose publicly. Requiring patentees to provide this information will facilitate compliance with the new, lower price ceilings that are expected to result from the new guidelines.

#### Patented Medicine Prices

	List Price		Rebates		Market Price
Current	✓	-	X	=	?
New	✓	-	✓	=	✓



# Despite small patient populations, EDRDs are a rapidly growing market, gaining sizable sales through high prices

## When less means more: Insight into spending on Expensive Drugs for Rare Diseases

An increasing number of expensive drugs for rare diseases (EDRDs) have emerged in recent years, bringing hope to patients suffering from life-threatening or debilitating conditions. Using sales data from IQVIA's MIDAS® Database, this analysis provides insight into Canadian and international EDRD markets, with information on pricing, sales, and market shares.

EDRDs are the fastest growing market segment in Canada, with 30% average annual increases in sales and a steady influx of new specialty medicines. In 2016 and 2017 alone, 23 oncology and non-oncology EDRDs were approved in Canada. Based on the profile of the drug pipeline, this trend expected to continue, with EDRDs becoming an increasingly significant driver of future pharmaceutical spending.

For the purpose of this study, EDRDs are defined as medicines with at least one orphan designation and estimated treatment costs exceeding \$100,000 per year for non-oncology drugs and \$7,500 per 28 days for oncology drugs.

### 1. An increasing number of EDRDs are being introduced, fueling this fast-growing market segment

Over the past several years there has been a substantial increase in the number of EDRDs and the spending on these medicines. The growth in EDRD expenditures is six times higher than the national growth rate observed for all prescription medicines in Canada – highlighting the growing importance of these drugs. The Canadian experience mirrors a wider global trend, with the 30% compound annual growth rate (CAGR) for EDRDs in Canada almost identical to the median OECD rate over the past seven years.

- Canadian sales of EDRDs reached \$1.8B in 2018, representing close to a 5-fold increase from \$0.4B in 2012.
- Oncology drugs represented a substantial portion of these medicines, accounting for close to 80% of EDRD sales over the past seven years.
- In 2018, the Canadian EDRD market share of total pharmaceutical sales reached 7%, 3.7 times greater than in 2012.

### 2. Affordability of drugs and sustainability of healthcare budgets are global issues

Payers globally are struggling to fund the increasing numbers of exorbitantly high-priced treatments. The cost of specialty drugs for cancer and rare diseases is threatening the sustainability of publically funded healthcare systems.

The low variation in pricing among countries suggests that international price referencing alone cannot address the challenges to affordability posed by these medicines. As a result, decision makers are increasingly using additional price control mechanisms to lower drug prices, with an increasing focus on the use of health technology assessment (HTA) tools.

- In 2018, Canadians spent \$50 per capita on EDRDs, marginally higher than the OECD median of \$44.
- Prices of EDRDs in Canada were among the highest in the OCED, ranking in 6th place; however, median foreign price levels were only 6% lower than Canadian levels and 12 countries had prices that were within 10% of Canadian levels.

### 3. EDRDs have the potential to generate the same revenues as lower-cost high-volume drugs

Manufactures argue that the relatively small market for EDRDs necessitates higher prices to recoup R&D costs and fund new developments. However, this analysis reveals that the revenue generating potential of EDRDs is comparable to that of high-volume medicines.

The analysis focuses on EDRD and non-EDRD medicines launched in Canada since 2005. The results are based on the highest annual sales attained for each medicine within three years of their launch date. Figure 3 illustrates the share of medicines with annual sales over \$10M, by increasing sales bands, as well as the corresponding share of sales revenue.

- 54% of EDRDs have more than \$10M in annual sales within the first three years after introduction, compared to 48% of non-EDRDs, which indicates that EDRDs have a higher probability of reaching larger sales revenues.
- Medicines with annual sales greater than \$10M account for 94% of the total sales for both EDRD and non-EDRD medicines.
- While a greater percentage of EDRD medicines have sales over \$10M, non-EDRDs have higher average annual sales, \$34M compared to \$28M.
- The median sales values for both EDRDs and non-EDRDs are approximately \$10M, with EDRDs having slightly higher median sales.

Non-EDRDs can be examined in more detail by breaking them down into groups of higher-cost medicines (with annual treatment costs ≥\$10,000) and lower-cost medicines (with annual treatment costs <\$10,000). The results show that in the first three years, only 44% of the lower-cost medicines have annual revenues exceeding \$10M – 10% less than for EDRDs – while 61% of the higher-cost medicines have annual revenues exceeding \$10M – 7% higher than for EDRDs.

A 2016 study by Hughes and Poletti-Hughes<sup>1</sup> found that EDRDs are five times more profitable than non-orphan drugs; in addition, according to our analysis, they can also achieve a comparable level of sales by the third year after launch.

### The Canadian experience echoes the message highlighted by the 2018 World Health Organization Technical Report on the Pricing of Cancer Medicines and its Impacts:



Figure 1: Canadian sales of EDRDs, 2012–2018

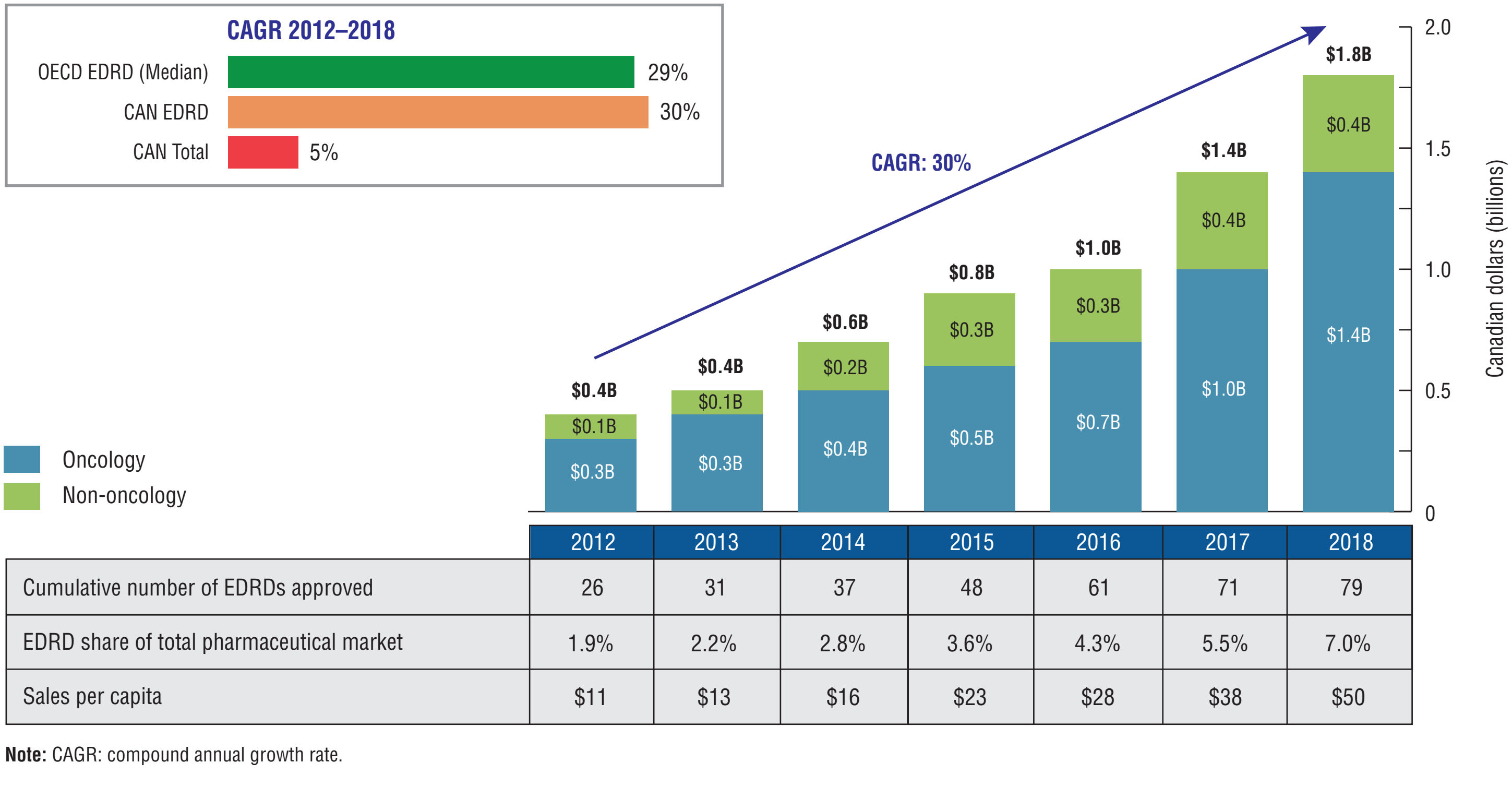


Figure 2: EDRD sales share, sales per capita, and price comparison, OECD countries

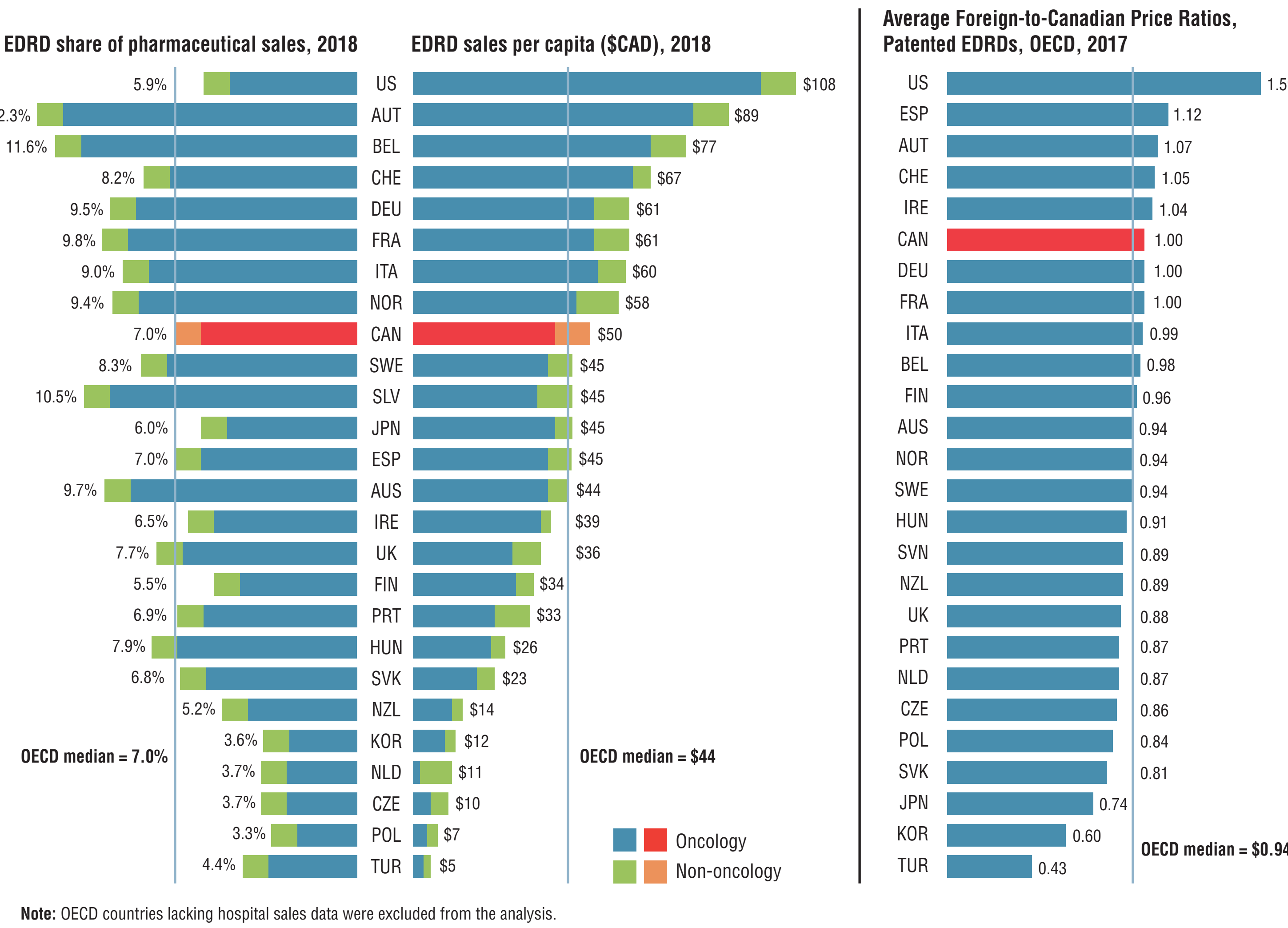
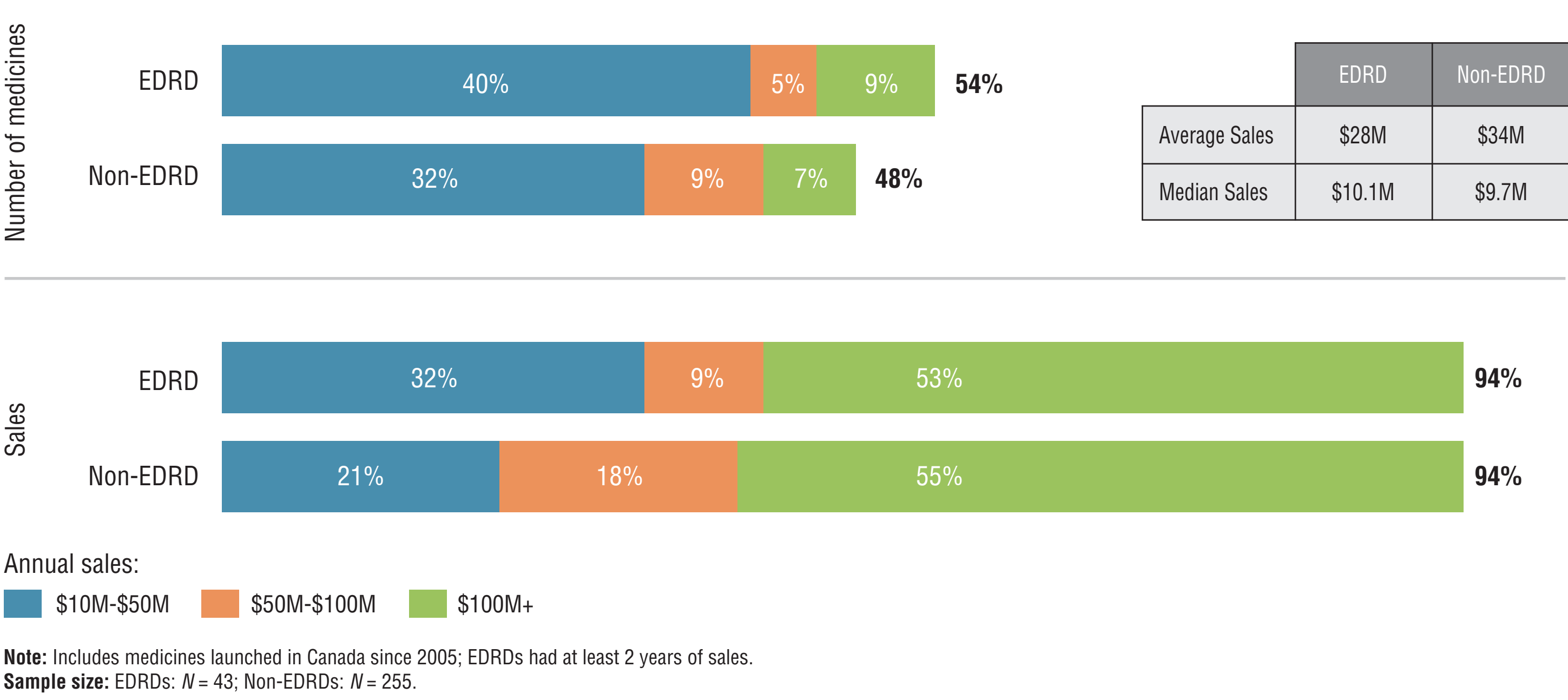


Figure 3: EDRD and non-EDRD distribution of medicines and of sales, by the highest annual sales in the first three years after launch in Canada



<sup>1</sup> Hughes D, Poletti-Hughes J. 2016. Profitability and Market Value of Orphan Drug Companies: A Retrospective, Propensity-Matched Case-Control Study. PLoS One. Oct 21;11(10):e0164681. doi: 10.1371/journal.pone.0164681.

Note: Results are based on list prices and do not capture off-invoice price rebates, managed entry agreements, or patient access schemes.

Data source: MIDAS® Database, IQVIA. All rights reserved.

For the Canadian market, MIDAS® data was supplemented with data captured by the PMPRB and IQVIA Private Pay Direct Drug Plan databases to ensure that all EDRDs authorized for sale in Canada were accurately identified.

Disclaimer: Although this information is based in part on data obtained under license from IQVIA's MIDAS® Database and Private Pay Direct Drug Plan databases, the statements, findings, conclusions, views, and opinions expressed in this study are exclusively those of the PMPRB and are not attributable to IQVIA.

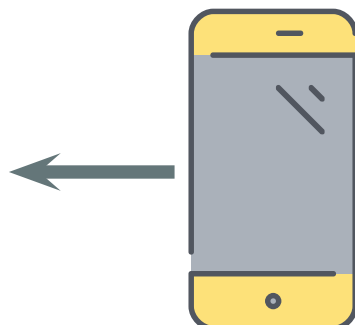
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# Well known processes from other industries have improved drug supply for hospital pharmacies

**Good practice to improve supply of hospital drugs and prevent backorders (tax funded, public sector)**

## Background and objective:

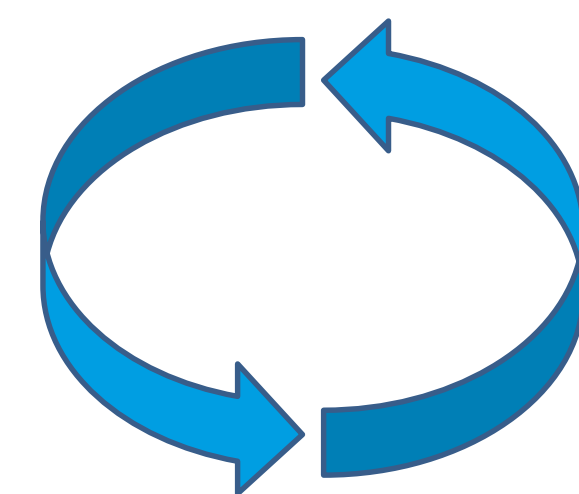
After years with an increasing number of backorders and many unplanned drug changes implemented under time pressure in the hospitals, we decided in 2017 to replace working in “firefighting mode” with being proactive through better supply chain transparency between hospital pharmacies and suppliers.

- The aim was to improve the supply of drugs to hospitalised patients in Denmark and to reduce the increasing number of backorder from suppliers

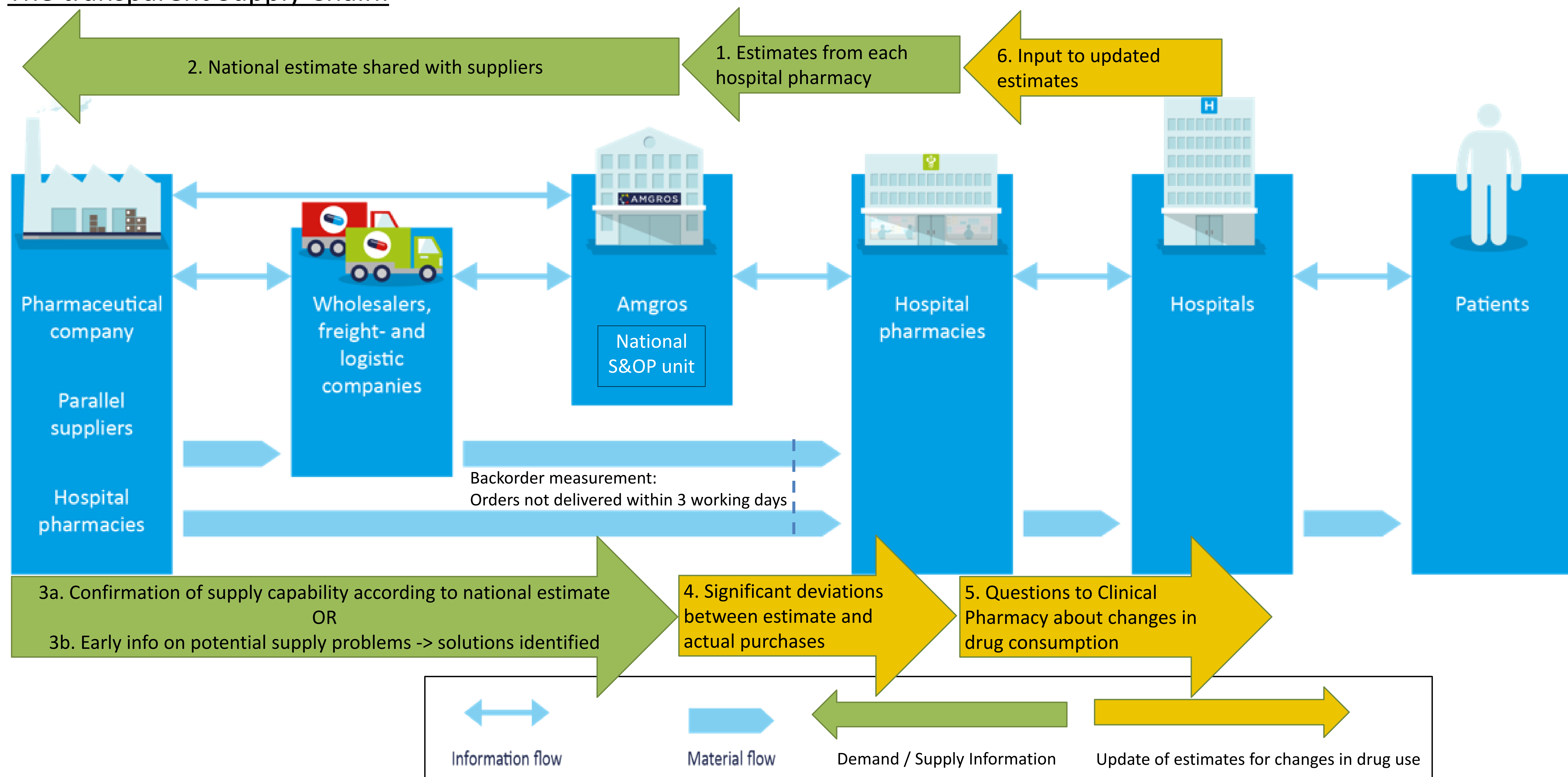
## Methodology

We established a national Sales & Operations Planning (S&OP) unit to develop and implement a national S&OP process for drugs on national tenders:

- All hospital pharmacies estimate their expected purchase volume [number of packages] on each item-number (Arrow 1 – on figure below)
- National estimates for each item-number are shared on a national supplier web portal. Suppliers are also advised about new estimates by e-mail (Arrow 2)
- On the national supplier web portal the suppliers confirm drug supply capability (Arrow 3a) or report potential supply problems (Arrow 3b)
- The national S&OP unit initiates and identifies proactive solutions for potential supply problems (Arrow 3b)
- Suppliers share production lead-time to give better understanding of their capabilities, e.g. to support planning of drug changes and decision making
- Monthly review process in place: Hospital pharmacies/clinical pharmacy update their estimates for changes in drug use (Arrows 4, 5 and 6)
- Suppliers re-confirm their supply capabilities, and national solutions are made for any identified supply problems (Arrows 1, 2, 3a and 3b)



### The transparent Supply Chain:



## How it was done

- I. **Involving** hospital pharmacies and suppliers in the step-by-step development of the S&OP process. **Helping** hospital pharmacies with estimation procedure
- II. **Help** to identify estimates that needed revision through quantitative and qualitative models, to improve estimate accuracy and supply security
- III. **Active communication** of estimates and revised estimates to suppliers
- IV. Rebuilding suppliers’ **trust** in our estimates as accuracy improved
- V. Asking suppliers to confirm supply capability and report potential supply problems proactively
- VI. Open and **cross-functional communication** about possible solutions to potential supply problems



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## Conclusions and lessons learned

- It’s hard work to implement a new focus area with many stakeholders, but be patient, maintain focus and results will show
- Positive feedback from both hospital pharmacies and suppliers on the benefits of participating in the national S&OP process. **A win-win situation.**
- Number of backorders have stabilised during 2017-2018 whilst other countries have experienced a sharp increase
- Transparency across the supply chain has generated trust and enabled more value adding and cross-functional dialogue e.g. sharing causes for estimate changes, supporting suppliers to get a reliable volume allocated to Denmark and early sharing of knowledge about potential supply problems
- Proactive solutions for potential supply problems have improved the overall supply situation, and have improved patient safety as fewer unplanned drug changes are implemented under time pressure

## Next steps

- Continue to improve the S&OP process and tools by involvement, support, active communication, trust and cross-functional communication
- Increased focus on education of clinical pharmacy staff and physicians, for them to give early warnings to hospital pharmacies prior to changes in drug use
- Help hospital pharmacies to predict changes in drug use, based on impact from national decisions about drug selection in the therapeutic areas



# The Italian Region Emilia-Romagna implements an evidence-based drug governance policy involving multi-stakeholder workgroups to promote equitable and sustainable access to drugs

## Drug Governance in the Emilia-Romagna Region, Italy



Francesco Nonino, Maria Chiara Silvani, Roberta Giroladini, Elisabetta Pasi, Lucia Magnano, Giulio Formoso<sup>1</sup>, Anna Maria Marata

Direzione Generale Cura della Persona Salute e Welfare, Servizio Assistenza Territoriale, Regione Emilia-Romagna, Bologna (Italy )  
WHO Collaborating Centre in Evidence-Based Research Synthesis and Guideline Development.  
<sup>1</sup> AUSL di Reggio Emilia, Reggio Emilia (Italy)

### Background

- The Italian National Health Service provides assessment, pricing and reimbursement of medicines through the Italian Medicines Agency (AIFA).
- However, each Italian Region can implement its own tailored drug governance policy within the national reimbursement regulation

### Methods

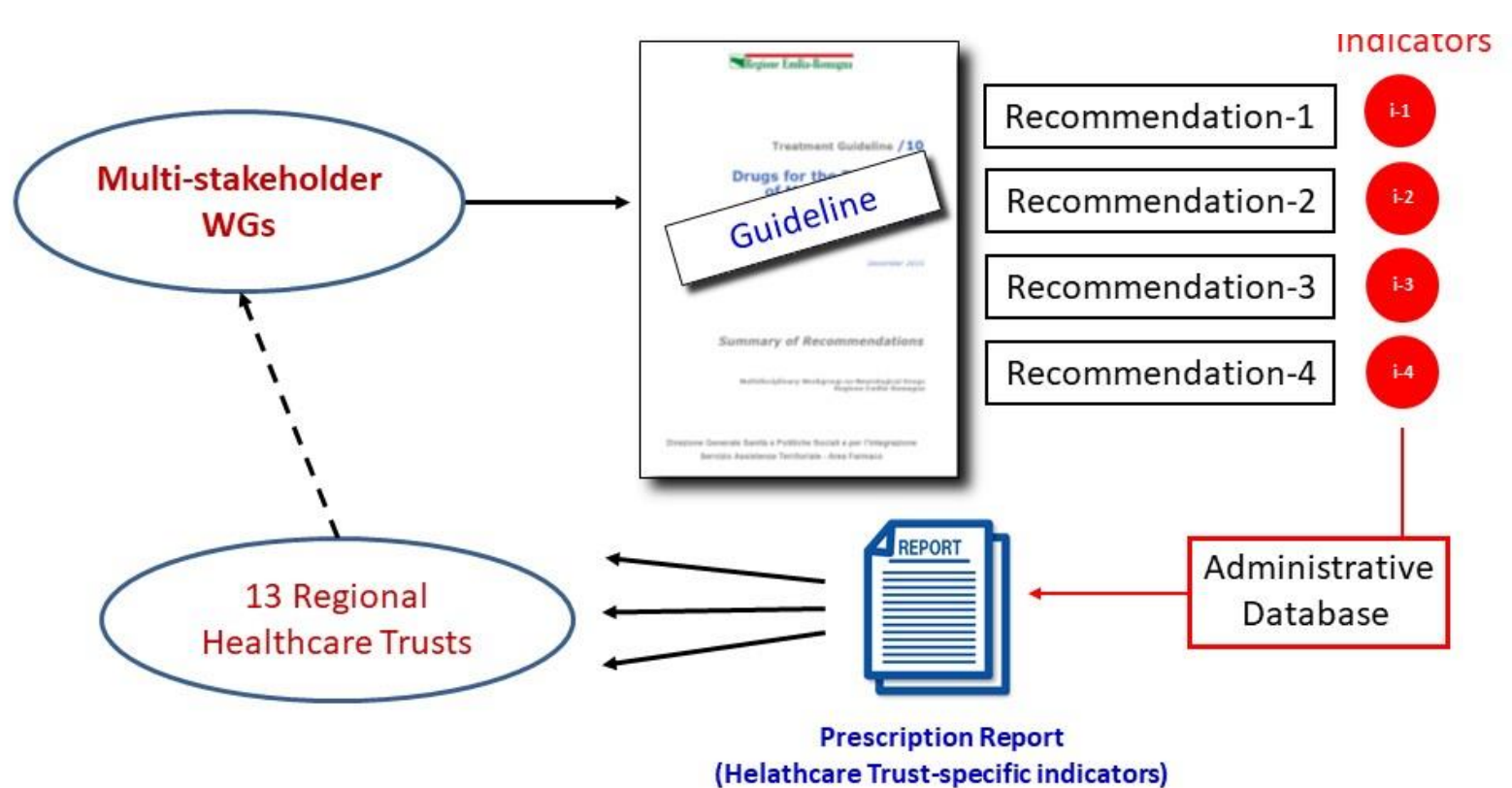
1. In the region Emilia-Romagna (RER) evidence-based recommendations on the use of medicines are issued by multi-stakeholder workgroups (MSWG), informing the decisions of a regional Drug and Therapeutic Committee (DTC) that monthly updates the Regional Drug Formulary (RDF)
2. Recommendations produced by means of the GRADE method are monitored through quantitative indicators expressing the expected prescription rates. **Yearly reports are produced for** conditions with high impact on resources
3. Drugs are purchased through centralized procurement procedures by a public independent regional agency.
4. Cost-opportunity evaluations to foster competition among pharmaceutical companies are part of RER’s drug governance policy

### Results

- **1,242** drugs included in the Regional Drug Formulary
- **255** documents on drugs issued by the DTC since 2006
- **79** with evidence-based recommendations and quantitative expected prescription rates
- **62** produced with the GRADE methodology
- **12** active workgroups

### Discussion

- RER implements a drug governance policy based on evidence-informed, structured, explicit and flexible guidance process involving MSWGs
- Differences between observed and expected prescription rates help understanding the determinants of variability among prescribers and can inform decisions about resource allocation.
- Appropriate use of drugs is key for the sustainability of a reimbursement-based system, warranting equitable access to treatments



Workflow of drug governance policy in the Emilia-Romagna Region (Italy)

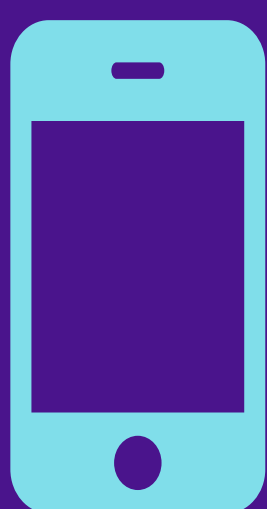
Strength/Direction	Definitions and implications	Expected prescription rate
<b>Strong Positive</b>	Most (although not ALL) patients should be offered the treatment. The recommendation could be used as a quality of care standard.	> 60-70%
<b>Weak Positive</b>	Wider range of uncertainty: it may indicate that only a relative minority of patients (30%) or a substantial proportion (50-60%) of patients should be offered the drug. Patients must be informed about expected desirable and undesirable consequences (and their magnitude), exploring their values and preferences and discussing possible alternatives	30-60%
<b>Weak Negative</b>	The treatment should be offered to a minority of patients or in selected cases. The decision should be thoroughly discussed with the patient about desirable and undesirable consequences of the treatment (and their magnitude), exploring their values and preferences and discussing possible alternatives	5-30%
<b>Strong Negative</b>	The treatment should not be routinely offered, not even to a subgroup of patients, but only in highly selected cases. The benefit/risk balance is unfavourable and safer alternatives are available.	< 5%

Translating GRADE’s «strength» and «direction» into prescription expected rates

Area	Active Multi-Stakeholder WGs	Topic	Specific guidance
Oncology	• GReFO (Gruppo Emiliano Farmaci oncologici)	Various onco-ematological malignancies	Various onco-ematology medications
Dermatology	• Psoriasis	Chronic plaque psoriasis	Multiple medical treatments, with focus on biologic drugs
Rheumatology	• Rheumatology (children and adults)	Spondylitis Ankylosans; Psoriatic Arthritis; Rheumatoid Arthritis; Juvenile Idiopathic Arthritis	Multiple medical treatments, with focus on biologic drugs
Gastroenterology	• Hepatitis-B	Hepatitis-B	Nucleos(t)ide analogues
	• Hepatitis-C	Hepatitis-C	Direct Antiviral Agents
	• Inflammatory Bowel Diseases	Inflammatory Bowel Diseases (ulcerative colitis, Crohn’s disease)	Multiple medical treatments, with focus on biologic drugs
Neurology	• Multiple Sclerosis	Multiple sclerosis not responding to interferon/glatiramer acetate	Monoclonal antibodies
	• Parkinson’s Disease	Parkinson’s disease	Dopamine receptor agonists Device-assisted medical treatments
	• Migraine	Episodic and chronic migraine (adults)	Monoclonal antibodies Botulinum toxin
Cardiovascular	• New Oral Anti-Coagulants	Preventive anticoagulation (non-valvular atrial fibrillation)	New Oral Anti-Coagulants
	• Acute Coronary Syndrome	Acute Coronary Syndrome (pre-admission and in-hospital management)	Antiplatelet agents
	• PCSK9	Hypercholesterolemia	PCSK9 inhibitors
Chronic Renal Impairment		Secondary hyperparathyroidism in chronic renal impairment (CKD-MBD)	Vitamin D, phosphate chelating agents, calcimimetics
Diabetes		Type 2 diabetes	Oral hypoglycemic agents in DM2 not controlled by metformine alone (DPP-4i, GLP-1a, SGLT2i)

Multistakeholder Workgroups in Emilia-Romagna

A full list of guidance documents (in Italian) is available at:  
<http://salute.regione.emilia-romagna.it/documentazione/ptr/linee-guida-e-raccomandazioni-ptr>



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# A drug governance policy incorporating **cost-opportunity** in evidence-based recommendations produced with the GRADE method

## Is cost-opportunity an effective strategy for drug expenditure governance? The experience on oncology drugs of the Emilia-Romagna Region, Italy



Lucia Magnano, Francesco Nonino, Roberta Giroladini, Elisabetta Pasi, Maria Chiara Silvani, Anna Maria Marata

Direzione Generale Cura della Persona Salute e Welfare, Servizio Assistenza Territoriale - Area Farmaco e Dispositivi Medici, Regione Emilia Romagna, Bologna, Italy - WHO Collaborating Centre in Evidence-Based Research Synthesis and Guideline Development



### Background

- High cost oncology drugs challenge the sustainability of healthcare systems.
- The Emilia-Romagna Region (RER) implements a drug governance policy by producing evidence-based recommendations and monitoring them through quantitative indicators.

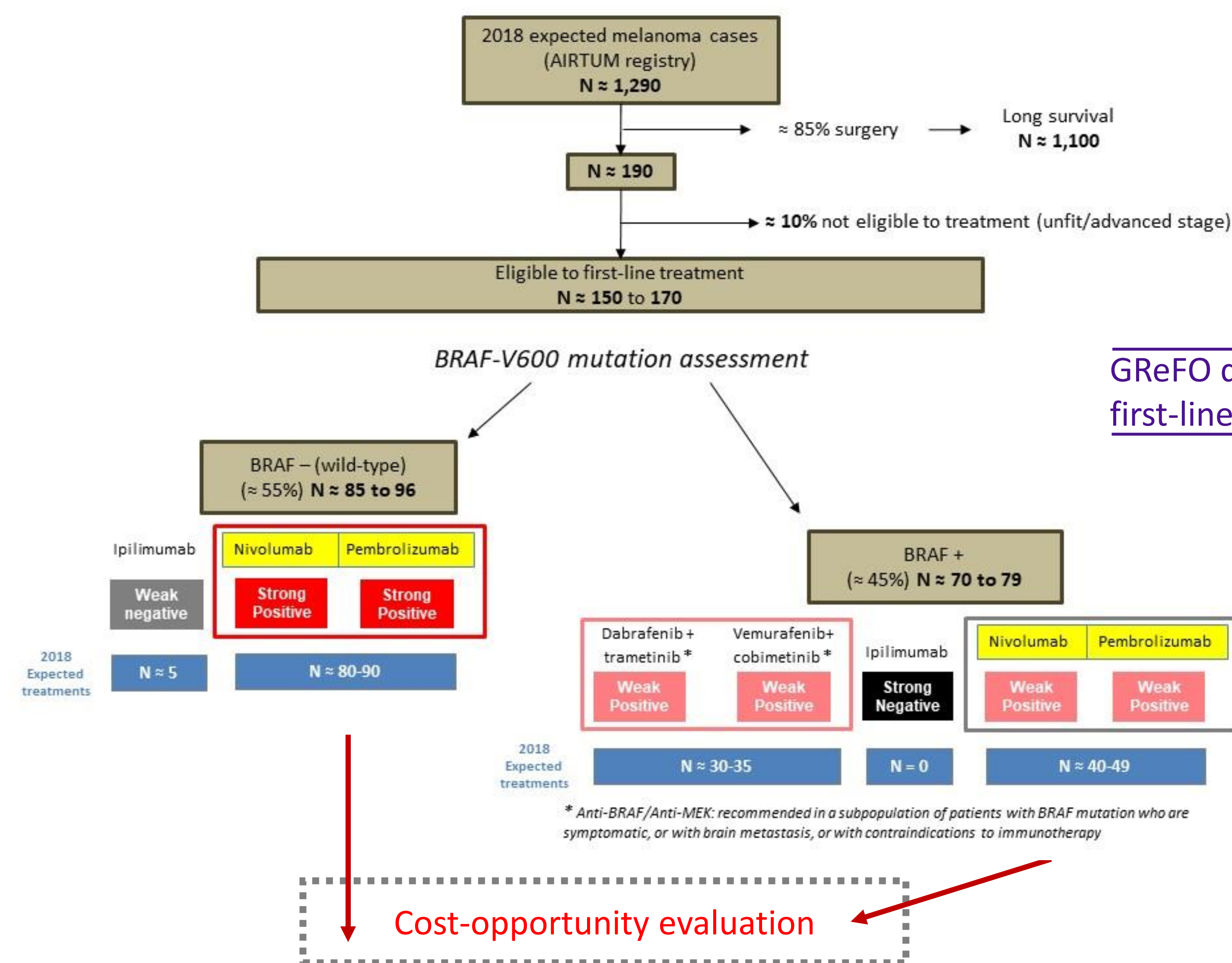
### Methods

- The GReFO (Gruppo Regionale Farmaci Oncologici) is a RER multi-stakeholder oncology workgroup producing guidance by means of the GRADE method [1].
- Although formal cost-effectiveness analysis is not performed, if drugs of the same class show no difference in terms of efficacy and safety, cost-opportunity (prescribing the least expensive drug) is recommended and prescription rates are formally monitored.
- The aim is to optimize the use of financial resources while warranting appropriate and equitable use of medicines, and to foster competition among drug companies.
- We describe the financial impact of implementing such policy to the first-line treatment of advanced stage melanoma (ASM).
- Expected melanoma cases and expected prescription figures were based on the Italian Association of Cancer Registries (AIRTUM) data and extrapolated from epidemiological studies.

### Results

- In 2017, licensed monotherapies for wild-type patients with ASM were nivolumab (Nivo), pembrolizumab (Pembro) and ipilimumab.
- Patients with the BRAF-V600 mutation (BRAF+) were eligible also to anti-BRAF/anti-MEK associations (BMAs).
- Recommendations with the same strength and direction were issued by GReFO for Nivo and Pembro in wild-type (strong positive) and in BRAF+ (weak positive) patients.
- According to cost-opportunity issues, GReFO recommended, within the immunotherapy class, the least expensive drug (Nivo) in BRAF+ patients.
- Considered for analysis: a sample of **154 ASM patients** (70% of the total) undergoing immunotherapy in 2018.
- 76%** and **24%** of ASM patients were treated with Nivo and Pembro, respectively. The overall expenditure was € 5,826,509 (rough figure, without considering the median duration of treatment).
- Compared with a hypothetical treatment of 50% of patients with each drug, adherence to cost-opportunity recommendation produced an **estimated saving of 5%** on the observed overall expenditure.
- Considering an adjusted cost/patient/year estimate, the savings may have been up to **11%**.

[1] Atkins D et al. BMJ. 2004 Jun 19;328(7454):1490



GReFO decisional pathway for the first-line treatment of ASM

Patients with ASM (N = 154) treated with Nivo and Pembro (2018)			
	Nivo	Pembro	Overall
Observed patients' distribution	<b>76%</b>	<b>24%</b>	
Observed expenditure	4,303,910	1,522,599	<b>5,826,509 €</b>
Hypothetical patients distribution (no cost-opportunity recommendation)	50%	50%	
Estimated expenditure	2,819,803	3,306,245	<b>6,126,018 €</b>
<b>Estimated difference</b>			<b>- 299,509 € (- 5 %)</b>

Adjusted estimates (considering cost/patient/year) for Nivo and Pembro in 154 ASM patients (2018)			
	Nivo	Pembro	Overall
Cost/patient/year	55,900 €	87,414€	
Observed patients' distribution	<b>76%</b>	<b>24%</b>	
Estimated adjusted expenditure	6,540,300 €	3,234,318 €	<b>9,774,618 €</b>
Hypothetical patients distribution (no cost-opportunity recommendation)	50%	50%	
Estimated adjusted expenditure	4,304,300 €	6,730,878 €	<b>11,035,178 €</b>
<b>Estimated adjusted difference</b>			<b>- 1,260,560 (- 11%)</b>

Prescription data on nivolumab and pembrolizumab, Emilia-Romagna, 2018

### Conclusions

- An evidence-based drug governance policy involving multiple stakeholders and sharing context-specific issues is feasible in a public healthcare system.
- Incorporating cost-opportunity issues in the production of evidence-based recommendations may result in substantial savings



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# Consider ways to enable ex-post analysis and evaluation of effective prices when Managed Entry Agreements terminate

Ex-post analysis of medicines subject to Managed-Entry-Agreements (MEAs) – a feasible approach for monitoring and price analyses  
Peter Schneider, Claudia Habl, Nemeth Gergely

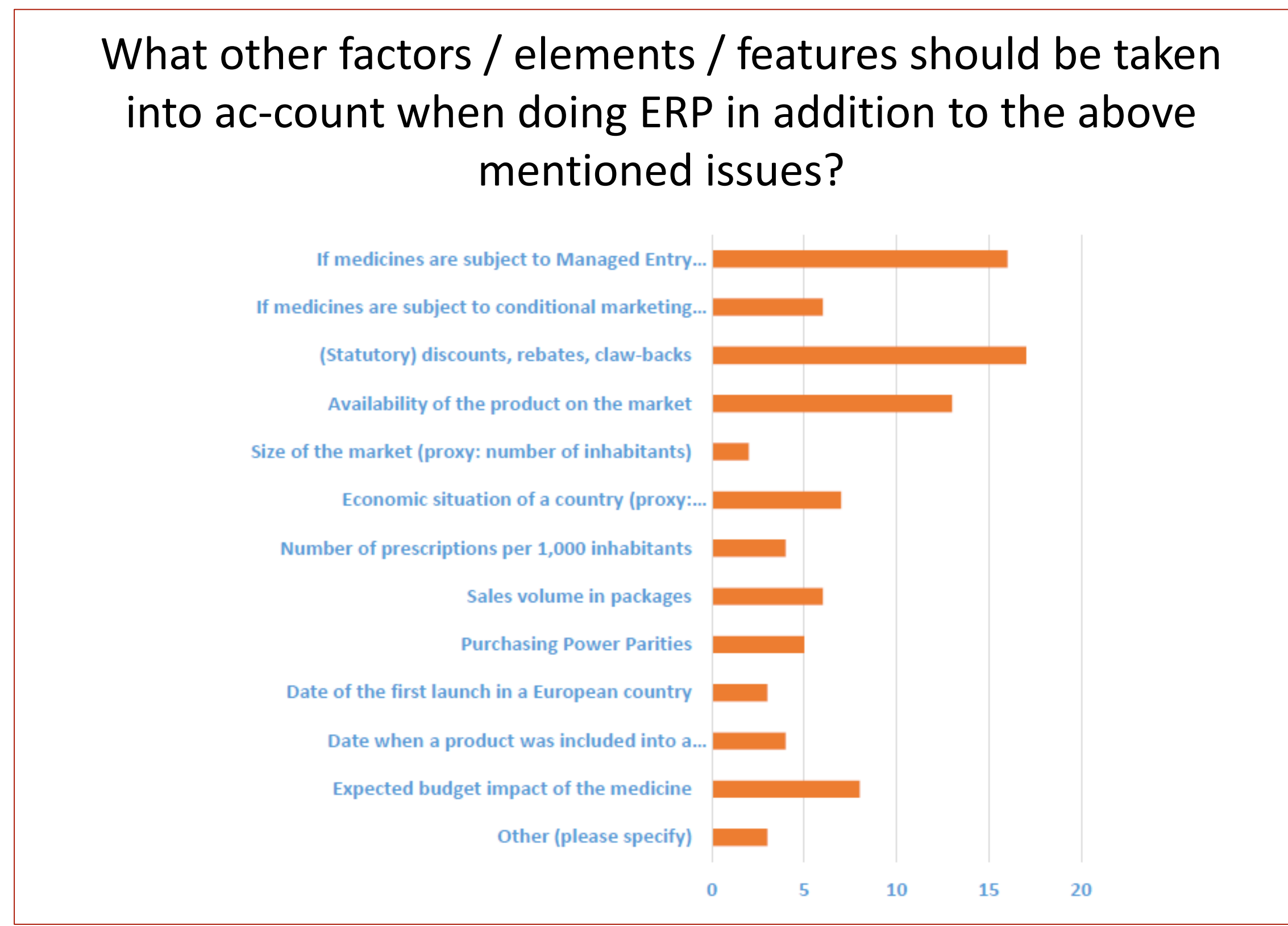
- Research in the field of medicine prices requires decisions on the methods applied in the study.
- The decisions on certain approaches are often determined by the study purpose, objectives and perspective, but the main goal is to make meaningful comparisons
- Aim: To assess which information competent authorities, researchers and stakeholder in the field of pharmaceutical pricing need when they conduct price analyses

Matrix of methods for price comparisons

At least > 1,000 options

Scope of countries	2	3	4	...	EU15	...	EU28		All OECD countries	Others	
Scope of products	1 product	Within a certain indication group (e.g. Oncology, chronic heart insufficiency)				Several products				"all" – Top selling products or generics, etc.	
Index construction	No	No (only listing)	Yes	No (only listing)	No (only average)	Yes	No (only listing)	Yes	No (only average)	Yes	10
Application of weights	No	No (only listing)	No (only Average)	Volume	No (only listing)	No (only average)	Volume	No (only listing)	No (only average)	Volume	
Unit of analysis	Same package ("like-by-like")		Standard unit		Gramm (of active ingredient)		DDD				4
Price type	Ex-factory price		Wholesale price / Pharmacy Purchasing price		Net Pharmacy Retail price (excl. VAT)		Gross Pharmacy Retail price (incl. VAT)				
	List price i.e. without discounts & rebates	Real prices i.e. price including discounts & rebates	List price i.e. without discounts & rebates	Real prices i.e. price including discounts & rebates	List price i.e. without discounts & rebates	Real prices i.e. price including discounts & rebates	List price i.e. without discounts & rebates	Real prices i.e. price including discounts & rebates			8
Price adjustments	No (daily exchange rate at date of survey)		No (exchange rate over a period)		Purchasing Power Parities (PPP)		GDP (per capita)				4

## Survey on information needs to conduct meaningful analyses/comparisons



- A needs assessment survey has been conducted among competent authorities and stakeholders in the field of pharmaceutical policy.
- The questionnaires contained 30 items and was structured in five overall topics.
- The questionnaire was distributed to 90 persons from 56 national and European institutions and associations.
- The survey was completed by 24 institutions (15 competent authorities for pricing and reimbursement, 9 international organisations, European associations of affected stakeholders and experts on pricing and reimbursement)

## MEA hamper meaningful analyses and comparison at any point in time

- Respondents emphasised the importance of making meaningful comparisons/evaluation of medicine prices
- The more information available, the more meaningful is the analysis
- Respondents identified information about the existence of Managed Entry Agreements (MEAs) and the type of MEAs as a supportive piece of information
- The practice of MEA has disrupted the informational value of prices and shattered established methods into pieces
- Current legal requirements do not allow monitoring or evaluation by third parties at any point in time

The Valletta group (Cyprus, Greece, Ireland, Italy, Malta, Romania, Portugal, Slovenia & Croatia) also pressed in 2019 for more transparency of prices of pharmaceuticals



Source: <https://www.independent.com.mt/articles/2019-07-12/local-news/Valletta-Deceleration-tackling-the-issue-of-transparency-on-medicine-prices-6736210821>

Gesundheit Österreich GmbH, Stubenring 6, 1010 Wien [www.goeg.at](http://www.goeg.at)

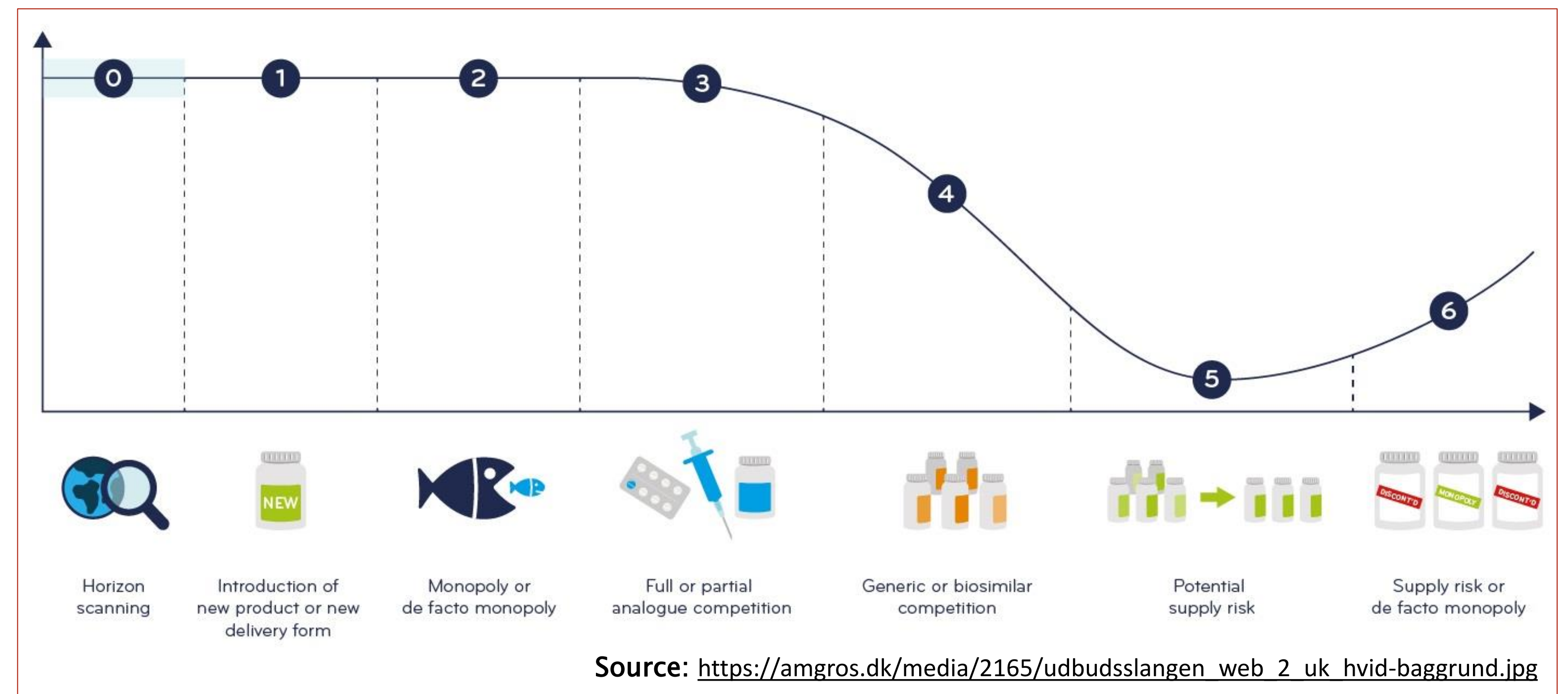


# Price developments of biological medicines do not correspond to estimated price levels

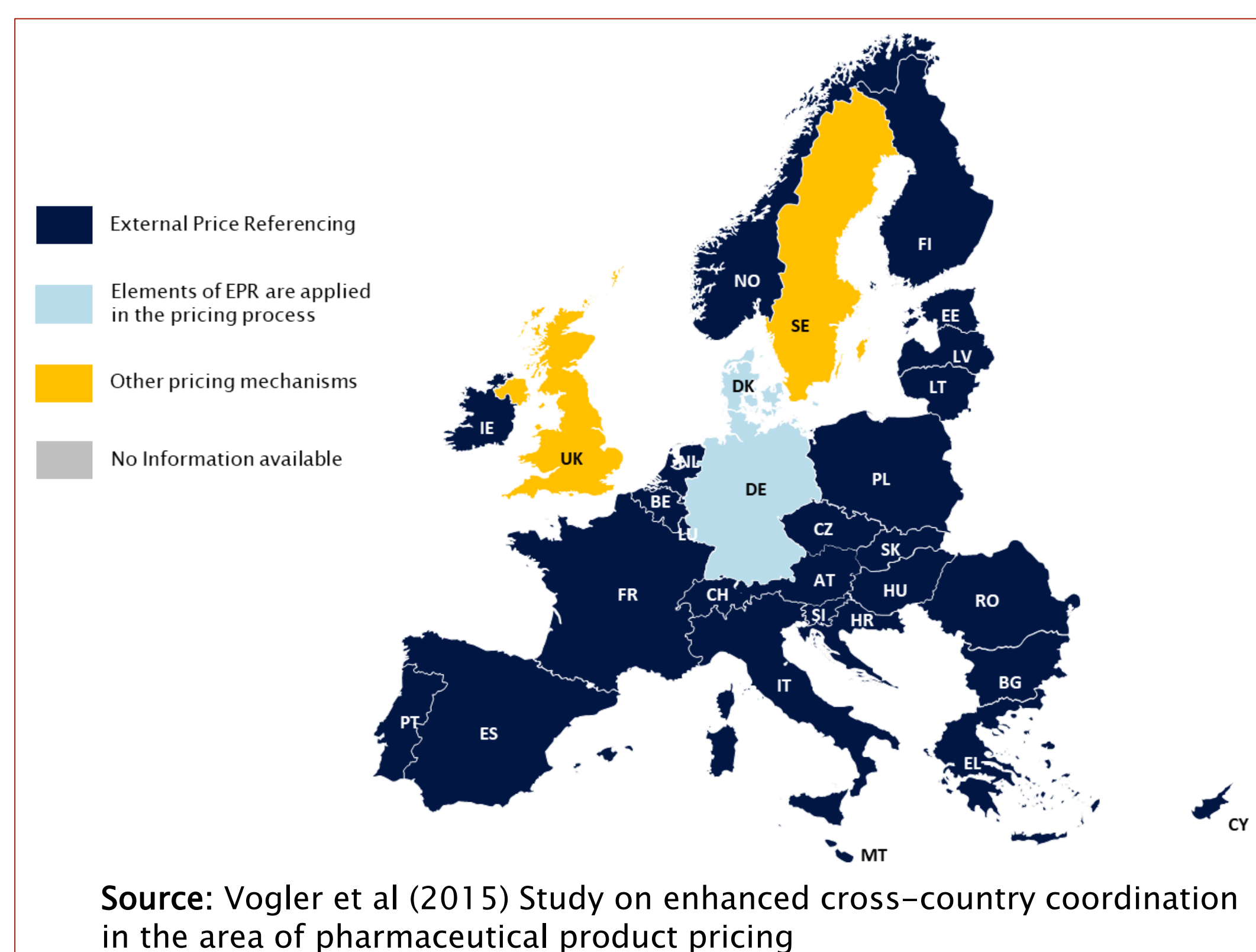
## Estimating price developments of biological medicines during market exclusivity

Peter SCHNEIDER, Lena Lepuschütz, Nina Zimmermann, Sabine Vogler

- A medicine passes through several different stages which is known as a 'product life cycle'
- Each stage is embedded in a regulatory and policy environment, which determines price dynamics
- Aim:** To estimate price developments of biological medicines during the stage of market exclusivity and compare these results with list prices of biologicals prior to the entry of the first biosimilar



## Survey results were used as inputs for a statistical model



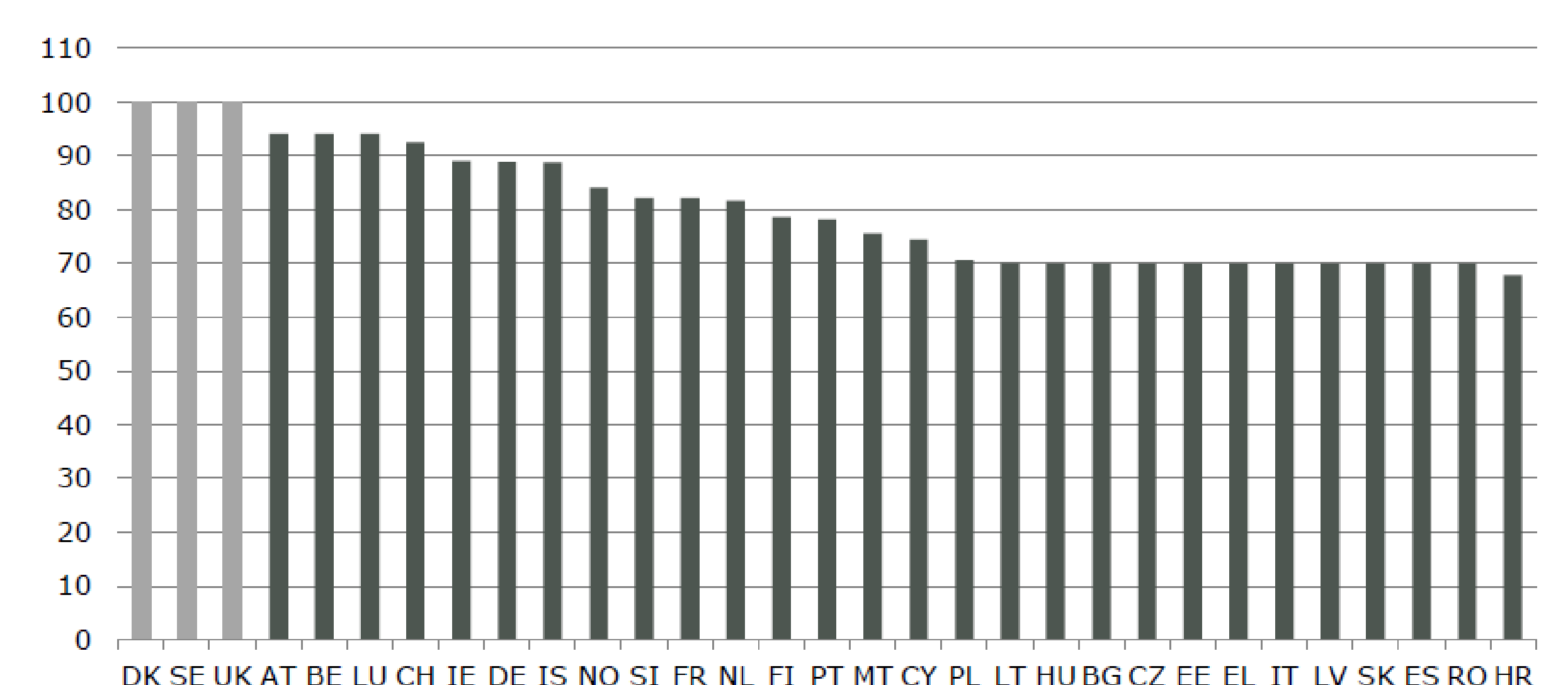
- Primary data collection on the use and practice of EPR, including detailed methodological information – among 30 European countries
- Results were used as inputs to model price developments through a discrete-event-simulation (DES)
- The model ran over a 10 year time horizon
- Pharma Price Information (PPI) service provided list prices of two biological medicines (Adalimumab and Rituximab) in the months before the first biosimilar entered the market



## The estimated average price was higher than the average of actual list prices

- The model predicted that after ten years, the average price level over the 30 countries was 80.2% of the starting price
- In the model, the highest price countries were Austria, Belgium, Luxembourg and Switzerland, while lower prices were predicted in Spain, Romania and Croatia
- In comparison to the model's estimations, the average price level of list prices was 66.8%
- The countries with the highest price level were Germany, Switzerland and Poland, while lowest prices were observed in UK, France and Greece

Estimated Ex-factory medicine prices after ten years



Source: Vogler et al (2015) Study on enhanced cross-country coordination in the area of pharmaceutical product pricing

Gesundheit Österreich GmbH, Stubenring 6, 1010 Vienna [www.goeg.at](http://www.goeg.at) & [https://ppri.goeg.at](http://ppri.goeg.at)



Substantial steps have been taken to improve the mechanism of developing the List of Reimbursement Outpatient Medicines, but further efforts will be need to be undertaken to achieve long-lasting changes in the area of transparency, relevance of decisions, revisability and implementation.

# Mechanism for introduction of outpatient medicines in the reimbursement list in the Republic of Moldova: development and challenges

Rita Seicas\*, Ghenadie Turcanu, Stela Bivol

## CONTEXT

In the context of global commitments to ensure extensive access to safe, effective, quality and affordable medicines, the assessment identifies barriers and factors that facilitate access to reimbursed medicines in the Republic of Moldova.

## OBJECTIVES

Objectives: The operational research of the national regulatory framework on developing the list of reimbursed outpatient medicines (LROM) by the mandatory health insurance funds aimed at identifying deficiencies and designing solutions for ensuring a transparent, holistic and feasible mechanism.

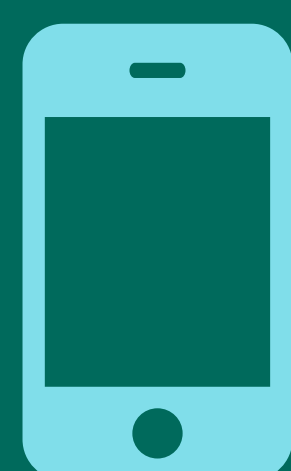
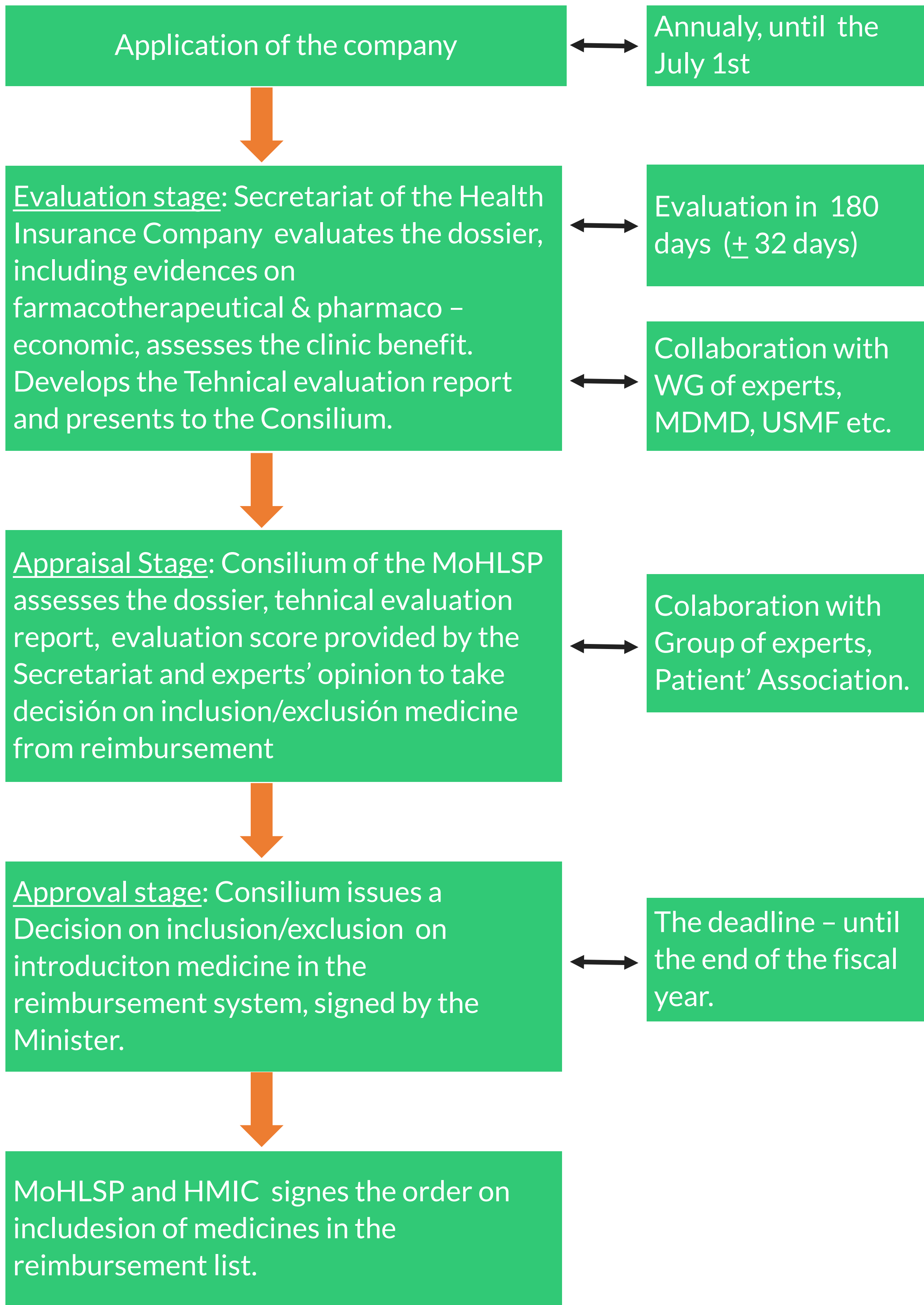
## METHODS

1. Analysis of the regulatory framework for outpatients medicines to be included in the list of reimbursed outpatient medicines (LROM).
2. Qualitative research of the opinions and perceptions of the beneficiaries of medicines and actors of the system.

## RESULTS

Mandatory health insurance implemented in the Republic of Moldova has shown to be an effective tool for improving the population's access to medicines. The LROM has evolved from 5 INN in 2005 to 148 INN in 2019. Public expenditures for LROM increased from 7403.5 thousand Moldavian lei (MDL) in 2005 to 523 859.3 thousand MDL in 2017. At the same time, the LROM did not significantly change compare to the national list of essential medicines. The first regulation on mechanism for introduction of outpatient medicines in the LROM was approved in 2010 and was revised fundamentally two times, with the most recent revision being done in 2015. The regulation was improved evidently, however, it is in need of further revision to:(1) improve transparency in establishing priorities for reimbursement; (2) re-introduce mandatory the cost-effectiveness criteria and budget impact analysis; (3) develop guidelines to enhance coherence and justifications of the process; (4) involve multidisciplinary expert teams. Qualitative research highlighted that access to LROM is perceived differently by different categories of population and actors of the system.

## Pathway of the application for approval of medicines for reimbursement by the Mandatory Health Insurance in Republic of Moldova



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# EML in Moldova is outdated. Public procurements show low share of EML out of LMCPP. This is a lost opportunity to ensure access and value for money and compliance with WHO EML.

## Assessing access to essential medicines list (EML) in the Republic of Moldova

Rita Seicas\*, Ghenadie Turcanu, Stela Bivol, Angela Carp

### CONTEXT

While Moldova has adopted policies on essential medicine list (EML), implementation has never been systematically reviewed. The PAS Center conducted a study on access to essential medicines

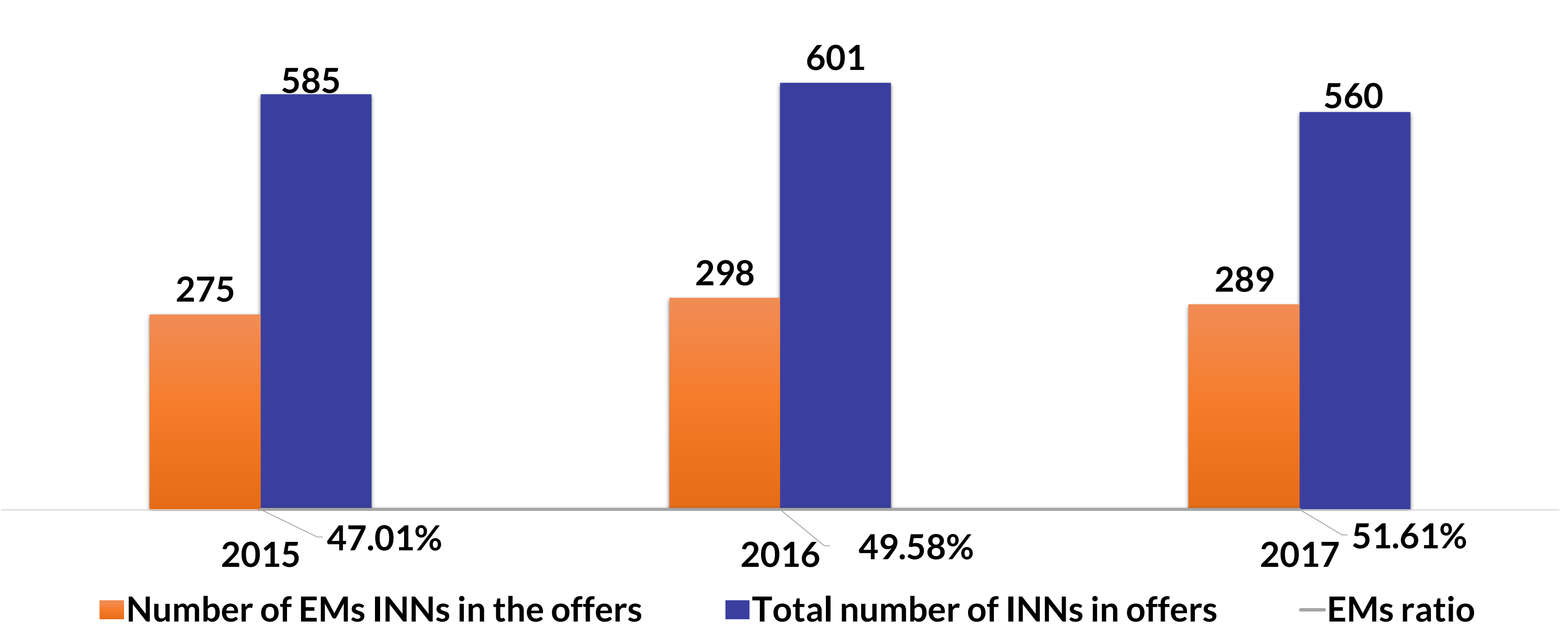
### METHODS

1. Analysis of national legislative and regulatory framework on essential medicines against international practices.
2. Analysis of alignment of the national EML (NEML) to WHO EML and reflection in the list of medicines of centralized public procurement (LMCPP).

### RESULTS

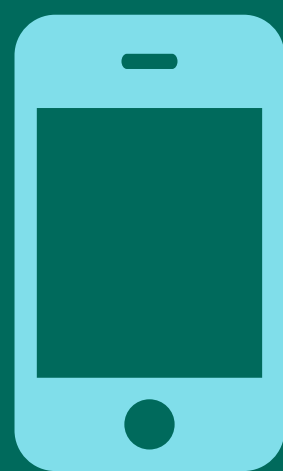
The first NEML approved in 1996 was revised four times, last one in 2011, which reveals that the number of medicines has expanded considerably. Comparative analysis of the NEML (635 molecules) with 2017 WHO EML reveals that 337 molecules are common to both lists, 152 molecules of WHO EML missing in 2011 NEML and 263 molecules of NEML not part of WHO EML. The LM CPP contains 52% of international non-proprietary names (INN) from EML (289 INNs out of a total of 560 procured INNs) in 2017, representing an improvement compared to 41% in 2011. Share of public budget for procurement of EML in the total contracted amount for public procurement of medicines has increased: from 43% in 2011 to 65.9% in 2017.

Year of NEML approval	Total number of molecules (excluding duplicates)	Total number of molecules (including duplicates)	Total number of pharmaceutical forms	Rate of pharmaceutical form per molecule	Total number of therapeutic categories
1996	106	108	147	1,36	0
2007	475	504	718	1,42	29
2009	519	578	819	1,41	27
2011	576	635	856	1,34	29



Year	2015*	2016	2017
a.Total number of INNs in the procurement list:	n/date	723 (100%)	603 (100%)
Total INNs with offers (procured)	585	83,13%(601)	92.87% (560)
Total INNs without offers	n/date	16.87% (122)	7.13% (43)
b.The total proportion of EMs/INNs in the procurement list:	n/date	43,43%(314)	49.92% (301)
Total INNs/ EMs with offers (procured)	275	94,90% (298)	96.01% (289)
Total procured INNs/ EMs without offers	n/date	5.10% (16)	3.99% (12)

Year	2015	2016	2017
The total number of bidded INNs (procured)	585	601	560
Number of bidded EMs/INNs (procured)	275	298	289
Rate of bidded EM/INNs, %	47.01%	49.58%	51.61%



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# A comprehensive policy framework conceived as a practical instrument to analyse and evaluate pharmaceutical systems, identify functional gaps, and choose reform interventions fitting the specific local needs and capacities

## A comprehensive pharmaceutical policy framework for decision-makers: functions, tools and data requirements

Ioana Ursu<sup>1</sup>, Viktoria Rabovskaja<sup>2</sup>

<sup>1</sup> Mapping Health Limited, London, UK

<sup>2</sup> GIZ GmbH, Eschborn, Germany

### PROBLEM STATEMENT

- World Health Report: medicines account for all three leading sources of inefficiency in health systems
- Moving towards UHC, countries face the impact of these inefficiencies on the health systems
- Various policy tools and methods have been developed - e.g. HTA, reference pricing, generic prescribing etc.
- There is limited guidance – specifically for low and middle-income countries decision-makers on which intervention, when and how to adapt to their specific country context

### OBJECTIVE

- Develop a comprehensive framework including the multitude of stakeholders and policies that form a pharmaceutical system
- The framework should provide a practical instrument for decision-makers and practitioners to:
  - evaluate their current system
  - identify functional gaps
  - choose reform interventions and tools fitting their specific country needs

### METHODS

- Multi-year, mixed methods work, across public & private sectors encompassing:
  - Desk review of policies, HTA assessments and qualitative interviews in 72 countries
  - Identified communalities of high income country systems
  - Results adjusted for middle-income settings (Eastern Europe)
  - Framework validated in Sub-Saharan Africa and South East Asia

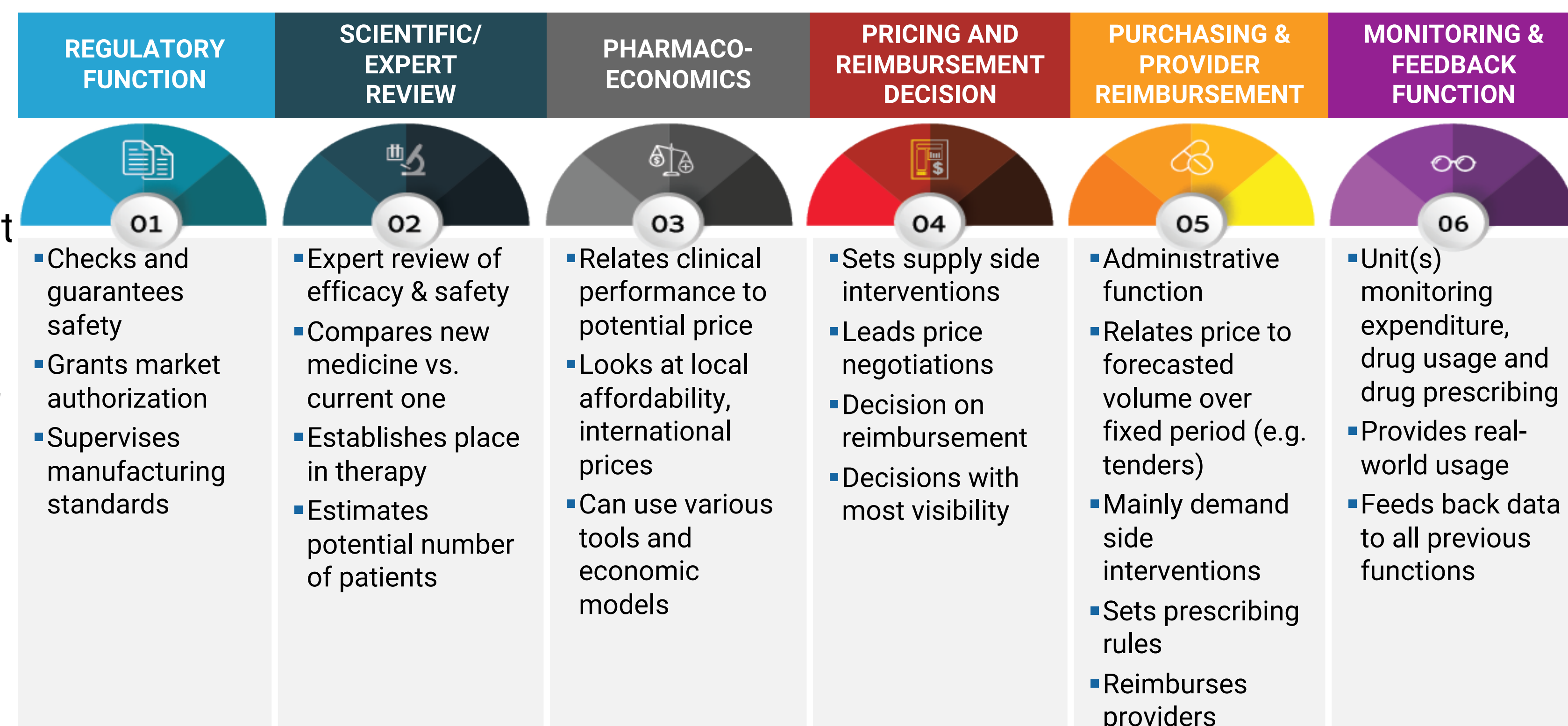
### COUNTRY EXPERIENCES

- The framework has been recently used in Indonesia, Philippines and Togo
  - In Indonesia, it identified the main drivers behind the persistent out of pocket spending despite the newly introduced social health insurance
  - In Philippines, the framework was used to create and integrate the HTA unit within Department of Health and develop the Primary Care Benefit package
  - In Togo, the framework helped develop a sustainable formulary and adjusted pricing method for the public health insurance

### THE FRAMEWORK – A STEP BY STEP APPROACH:

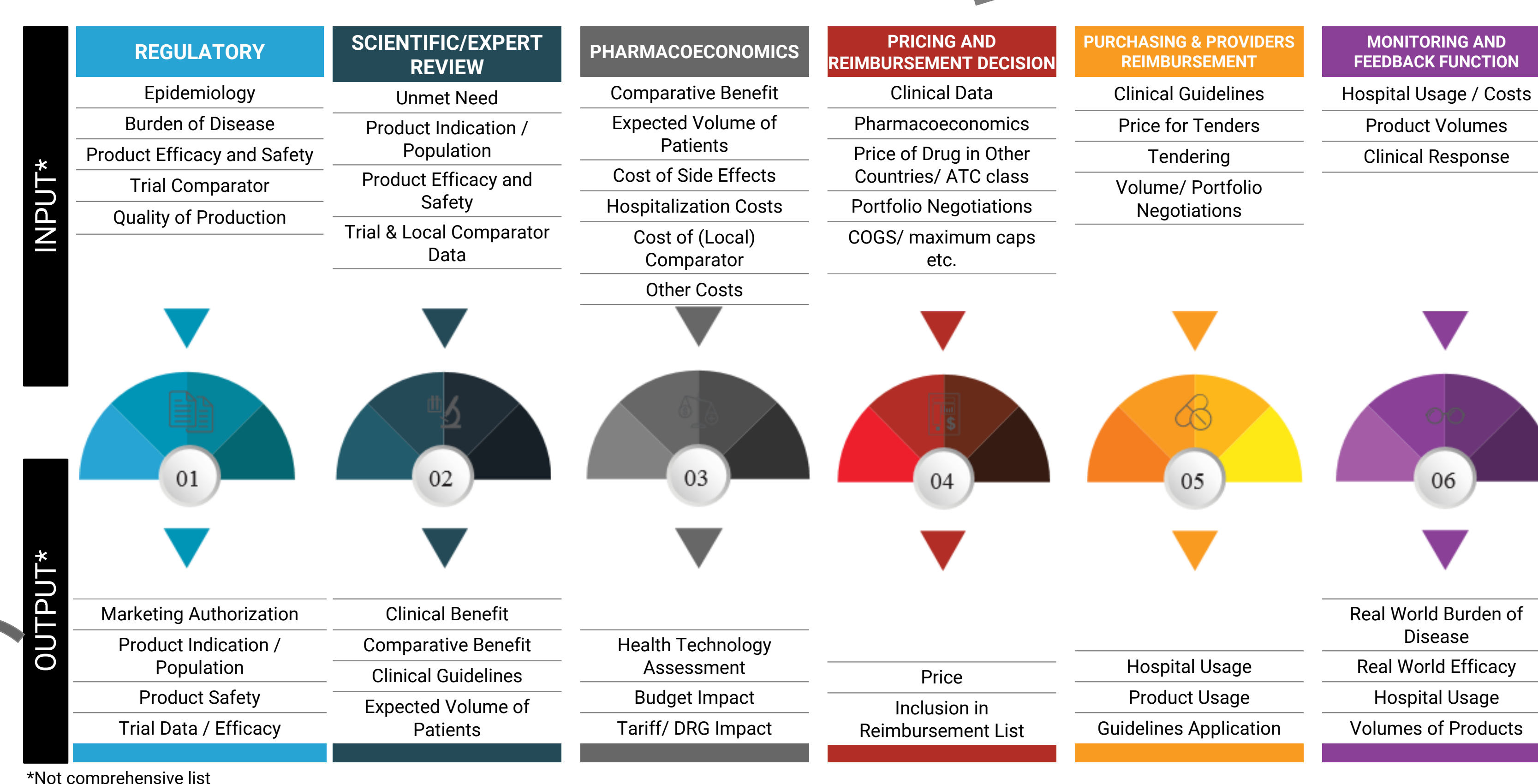
- Evaluate if the six mandatory functions of the system are present

➤ *Optimal:* all functions should be present, even if multiple institutions fulfil them



- When all functions are present, a very well defined sequence between the functions is needed to ensure optimal decision efficiency, starting from regulatory and ending with the monitoring and feedback function

- To ensure optimal system operations, each function should have a specific set of data and tools used, with the output generated by one function used as input by the next one



- The flow of information should be organised as a continuous process
- Feedback should be continuously available on volumes used, epidemiology, mortality and morbidity drivers, uptake of the new treatment, efficacy in real world settings, costs etc.

**CONCLUSION** The framework proposes a general approach that to be applied across low, middle and high-income settings. It helps decision-makers and technical staff analyse and envisage how the pharmaceutical system could be improved given the local context data availability and human capacity.

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# Different methodological approaches of external price referencing lead to different medicine prices.

## O09: Impact of the external price referencing (EPR) methodology on medicine prices – Simulation of existing EPR models

### Background

- External price referencing (EPR) is a frequently used medicine pricing policy
- It aims to lead to more affordable (lower) prices
- Different dimensions are to be taken into consideration when designing an EPR system, e.g.
  - Basket of reference countries
  - Calculation of the benchmark price
  - Exchange rate
  - Weighting price data of reference countries

### Objective

- To investigate the impact of changes in the EPR methodology on medicine prices (list prices)

### Methods

Parameter	Methodological approaches
Model	Discrete-event simulation (DES)
Price data	Fictitious prices
Countries included	All 28 EU Member States except Denmark, Sweden and UK; plus Iceland, Norway and Switzerland
Time period	Period of 120 months, starting Q1 /2015
Base case	“Real-life setting”: Dimensions of EPR in the countries as in place in 2015, as surveyed
Simulations	Different scenarios were simulated
Assumptions	Prices were held constant until a re-evaluation was due according to legislation No consideration of price deflation/ inflation Exchange rates were held constant EPR was assumed to be the sole pricing policy in the EPR-applying countries Launch countries: Germany (assumed price: 100) and Italy (assumed price: 70)

### Findings

Countries	Base case	Discounts	Revisions (every 6 months)	PPP adjustment	Basket change (4 countries)	Basket change (30 countries)	Minimum price	Exchange rate (yearly)	Exchange rate (monthly)
AT	94.0	82.0	76.5	88.2	94.0	85.0	70.0	94.0	94.6
BE	94.0	82.0	76.5	88.9	94.0	85.0	70.0	94.0	94.6
BG	70.0	19.0	69.5	32.9	67.5	83.9	54.7	62.5	58.1
CH	93.0	66.0	86.5	129.5	77.1	84.2	62.3	95.8	98.2
CY	74.0	47.0	70.0	57.6	66.2	72.4	48.0	75.6	76.3
CZ	70.0	35.0	69.5	45.5	67.8	83.9	56.2	62.7	58.1
DE	89.0	72.0	79.9	80.0	87.7	85.0	77.9	88.9	90.4
EE	70.0	32.0	69.5	50.6	67.8	83.9	56.0	62.8	59.2
EL	70.0	22.0	69.5	58.0	67.5	83.9	54.7	62.6	59.0
ES	70.0	29.0	69.5	62.5	67.5	83.9	55.8	62.7	59.3
FI	78.6	37.2	74.7	87.0	74.6	81.5	52.7	91.2	91.8
FR	82.2	34.5	79.7	82.8	76.9	84.2	54.7	90.0	90.3
HR	67.8	11.4	65.7	41.1	70.5	77.0	50.1	66.4	63.1
HU	70.0	56.0	69.5	35.6	70.0	70.0	70.0	62.5	61.1
IE	89.1	59.2	82.5	82.9	77.1	84.2	57.3	91.3	92.0
IS	88.8	72.8	84.8	91.9	73.6	80.6	54.7	99.4	99.3
IT	70.0	23.2	69.5	70.0	67.5	83.9	54.7	65.0	59.7
LT	70.1	13.7	69.5	42.2	77.0	84.2	55.8	64.4	61.6
LU	94.0	82.1	76.5	95.7	67.5	83.9	70.0	94.0	94.6
LV	70.0	34.5	69.5	47.1	67.5	83.9	54.7	65.2	62.4
MT	75.5	25.2	74.0	55.4	77.1	84.2	56.2	74.0	72.0
NL	81.6	55.4	75.1	75.1	68.8	75.3	56.3	84.8	86.5
NO	84.0	50.5	73.1	99.4	63.7	78.9	53.9	87.4	80.2
PL	70.6	16.4	69.8	40.6	76.9	84.2	54.7	67.2	64.7
PT	78.2	22.2	75.2	56.1	77.0	84.0	55.8	81.9	79.9
RO	70.0	18.5	69.5	34.4	67.5	83.9	54.7	66.4	64.7
SI	82.2	32.1	76.5	58.9	67.5	83.9	63.0	90.0	90.3
SK	70.0	24.3	69.5	47.1	67.5	83.9	54.3	62.6	59.2
Ø price / base case	78.1	41.2 - 47.2%	73.6 - 5.8%	65.6 - 16.0%	73.0 - 6.5%	82.2 + 5.3%	58.2 - 34.2%	77.3 - 1.0%	75.8 - 3.0%

### Base case (continuation of 2015 methodology):

- 21.9% after 10 years

### Simulations with highest impacts:

- Consideration of discounts (assumed 20% discount in 6 large economies and mandatory discounts in DE, EL & IE): -47.2%
- Calculation based on lowest price in ref. countries: -34.2%

### Simulations with mixed impacts:

- Adjusting price data to PPP: -16%

### Simulations with further impacts:

- Regular price revisions
- Changes in the basket of reference countries
- Shorter intervals of the average exchange rates

### Conclusions

- The methodological design of EPR can result in (partially substantial) changes of the price
- Savings for payers through strategic choices



### Acknowledgements go to

- Lena Lepuschütz, GÖG for her collaboration in the study &
- PPRI network members for providing data for the base case.
- This analysis was part of a larger study funded by the Health Programme of the European Union (see QR code), we acknowledge the funding of the European Commission.

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# For on-patent medicines one presentation per active ingredient can be sufficient for a price comparison.

## P18: Choosing the right medicines for price comparisons Analysis of prices of pharmaceutical presentations of the same active ingredient

### Background

- Selecting medicines for international price comparison is a major challenge
- *Is it sufficient to select one single pharmaceutical presentation to represent the active ingredient or should all presentations of an active ingredient be included?*

### Objective

- To analyse the prices of different pharmaceutical presentations of the same active ingredient in European countries
- with a view to assessing possible differences between them

### Methods

Parameter	Methodological approaches
Medicines selected	22 active ingredients (at least 1 presentation per active ingredient among high-cost medicines for Austrian public payers in Q2/2017); at least 2 presentations per active ingredient studied
Countries	27 countries (all 28 EU Member States except Malta)
Data source	Pharma Price Information (PPI) service of GÖG
Survey date	September 2017
Analysis	ex-factory prices (list prices, before discounts) per unit (e.g. tablet, vial)

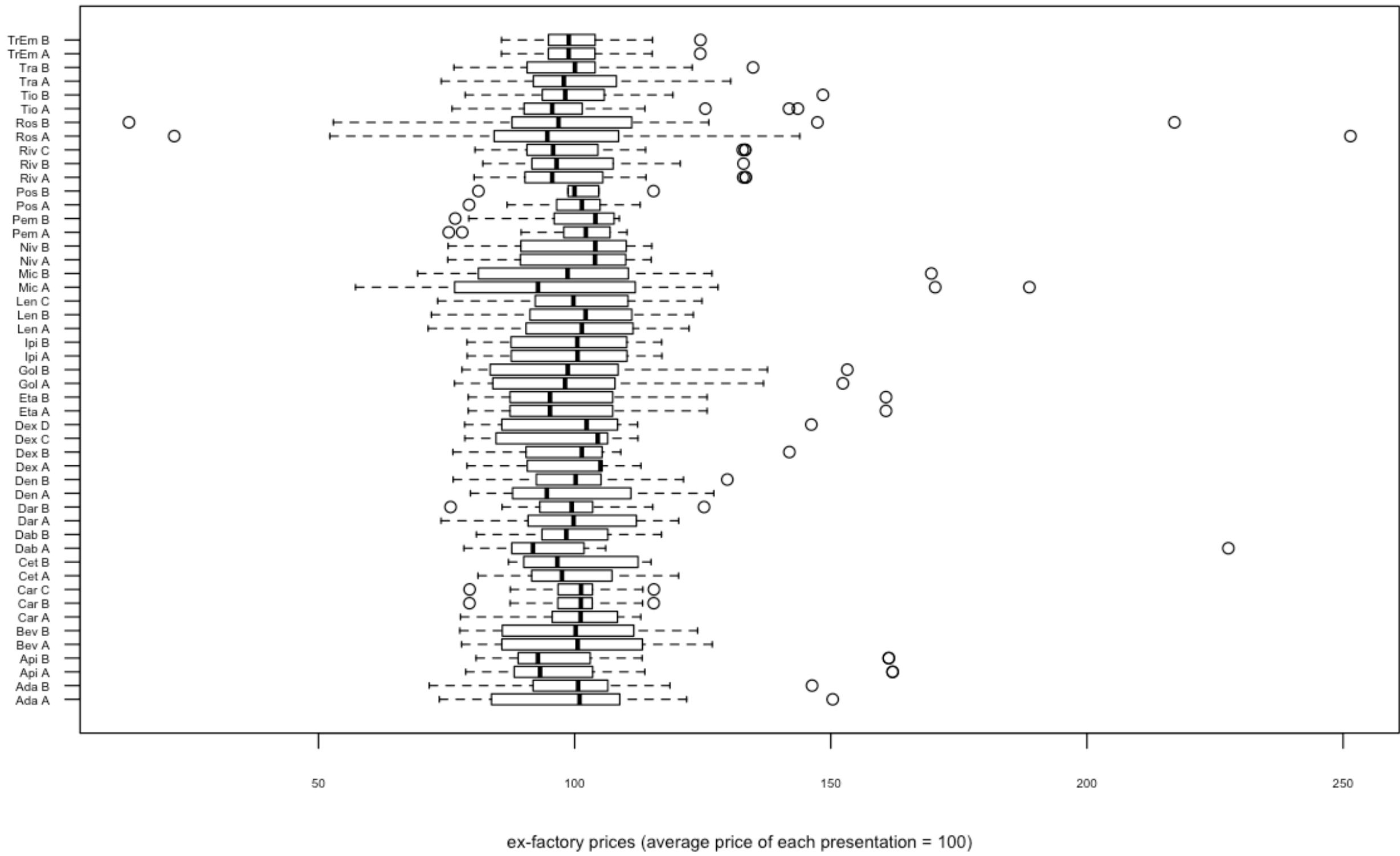
## Findings

### Same prices of different presentations of an active ingredient

- For 18 of the 22 studied active ingredients, the per unit ex-factory prices were the same for the surveyed pairs of the pharmaceutical presentations in several countries
- The relative ranking of unit prices across the European countries did not differ considerably between presentations of the same active ingredient

### A different pattern was found in cases

- of the marketing of different presentations for different indications (denosumab) and
- of emerging generic competition, which also impacted originator prices (rosuvastatin)



## Conclusions and lessons learned

- The findings suggest that **for on-patent medicines the inclusion of a single presentation per active ingredient in a price comparison can be sufficient**, since prices or ranking of those do not differ substantially.
- As soon as **generic competition** starts, however, price dynamics will likely occur, and **it is recommended including further pharmaceutical presentations of an active ingredient** in a price study.

### Funding

- This is a follow-up analysis of a medicine price study performed for the Austrian Federal Ministry of Labour, Social Affairs, Health and Consumer Protection (BMASGK), see *QR code*.
- The Pharma Price Information (PPI) service, from which medicine price data were sourced, is financially supported by BMASGK.

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### How to read the box plot:

The average price of each presentation is defined as an index (= 100). The box corresponds to the area in which the middle 50% of the data are located (interquartile distance). The black line describes the location of the median. The dashed whiskers are limited to 1.5 times the length of the interquartile range. The circles stand for statistical outliers.

### Included presentations

Ada = adalimumab 40 mg, 0.8 ml, injection for solution, 2 pre-filled syringes (A), adalimumab 40 mg, 0.8 ml, injection for solution, 2 pre-filled pens (B); Api = apixaban 2.5 mg, 60 f/c tablets (A), apixaban 5 mg, 60 f/c tablets (B); Bev = bevacizumab 100 mg / 4 ml concentrate to produce a solution for infusion, 1 vial (A), bevacizumab 400 mg / 16 ml concentrate to produce a solution for infusion, 1 vial (B); Car = carfilzomib 60 mg / 30 ml powder for solution for infusion, 1 vial (A), carfilzomib 10 mg / 5 ml powder for solution for infusion, 1 vial (B); Car = carfilzomib 30 mg / 15 ml powder for solution for infusion, 1 vial (C); Cet = cetuximab 100 mg / 20 ml solution for infusion, 1 vial (A), cetuximab 500 mg / 100 ml solution for infusion, 1 vial (B); Dab = dabigatran etexilate 110 mg, 30 hard capsules (A), dabigatran etexilate 150 mg, 30 hard capsules (B); Dar = daratumumab 100 mg / 5 ml concentrate to produce a solution for infusion, 1 vial (A), daratumumab 400mg / 20 ml concentrate to produce a solution for infusion, 1 vial (B); Den = denosumab 60 mg / 1 ml solution for injection, 1 pre-filled syringe (A), denosumab 120 mg / 1.7 ml solution for injection, 1 vial (B); Dex = dexamethasone 200 mcg / 2 ml concentrate to produce a solution for infusion, 5 ampoules (A), dexamethasone 200 mcg / 2 ml concentrate to produce a solution for infusion, 25 ampoules (B); Eta = etanercept 50 mg / 1 ml solution for injection, 4 pre-filled syringes (A), etanercept 50 mg / 1 ml solution for injection, 4 pre-filled syringes (B); Gol = golimumab 50 mg / 0.5 ml solution for injection, 1 pre-filled pen (A), golimumab 50 mg / 0.5 ml solution for injection, 1 pre-filled syringe (B); Ipi = ipilimumab 50 mg / 10ml concentrate to produce a solution for infusion, 1 vial (A), ipilimumab 200 mg / 40 ml concentrate to produce a solution for infusion, 1 vial (B); Len = lenalidomid 10 mg, 21 hard capsules (A), lenalidomid 15 mg, 21 hard capsules (B); Mic = micafungin 50 mg / 10 ml powder for a concentrate to produce a solution for infusion, 1 vial (A), micafungin 100 mg / 10 ml powder for a concentrate to produce a solution for infusion, 1 vial (B); Niv = nivolumab 40 mg / 4 ml concentrate to produce a solution for infusion, 1 vial (A), nivolumab 100 mg / 10 ml concentrate to produce a solution for infusion, 1 vial (B); Pem = pembrolizumab 50 mg / 2 ml powder for a concentrate to produce a solution for infusion, 1 vial (A), pembrolizumab 100 mg / 4 ml powder for a concentrate to produce a solution for infusion, 1 vial (B); Pos = posaconazole 100 mg, 24 enteric tablets (A), posaconazole 100 mg, 96 enteric tablets (B); Riv = rivaroxaban 20 mg, 30 film-coated tablets (A), rivaroxaban 20 mg, 30 film-coated tablets (B); Ros = rosuvastatin 10 mg, 30 film-coated tablets (A), rosuvastatin 20 mg, 30 film-coated tablets (B); Tio = tiotropium bromid 18 mcg inhalation powder, 30 capsules (A), tiotropium bromid 2.5 mcg inhalation solution, 1 inhaler (B); Tra = trastuzumab 150 mg / 7.2 ml powder for a concentrate to produce a solution for infusion, 1 vial (A), trastuzumab 120 mg / 5 ml a solution for injection, 1 vial (B); TrEm = trastuzumab emtansine 100 mg / 5 ml powder for a concentrate to produce a solution for infusion, 1 vial (A), trastuzumab emtansine 160 mg / 8 ml powder for a concentrate to produce a solution for infusion, 1 vial (B)





The design of pricing and reimbursement policies varies greatly across PPRI member countries. For conclusions on access to medicines further research is needed.

## Comparative analysis of pharmaceutical pricing and reimbursement policies in 47 PPRI member countries

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Report will be published soon at <http://ppri.goeg.at>

### Background

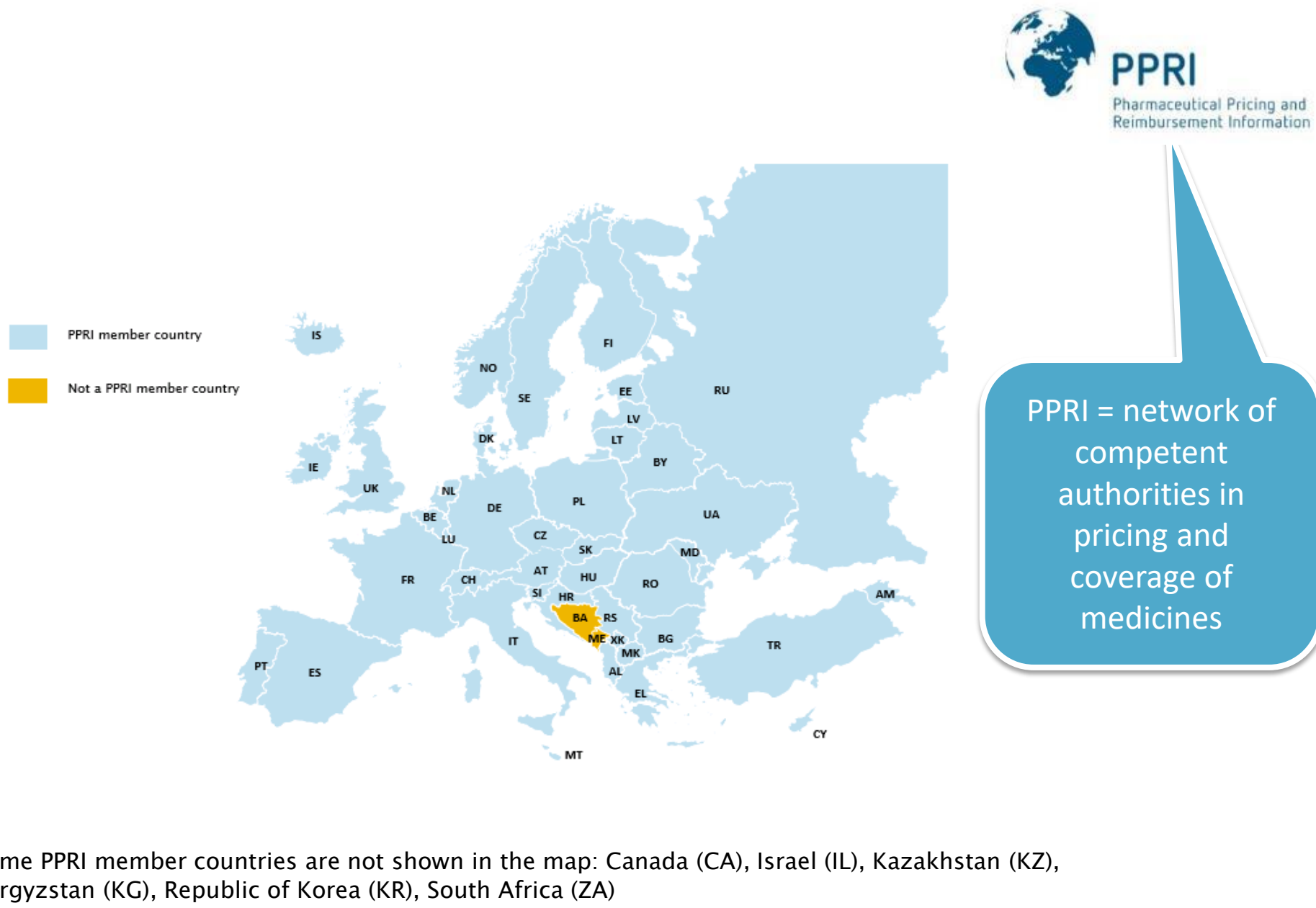
- Knowledge of appropriate measures, including methodological aspects and practice experience, in other countries as well as evidence of their impacts are of major importance for policy-makers

### Objective

- To offer a comprehensive, concise and up-to-date comparative analysis of pharmaceutical pricing and reimbursement policies implemented in the outpatient and inpatient sectors in the 47 member countries of the PPRI network

### Methodology

- Primarily through primary surveys of competent authorities in 47 PPRI member countries
- Additional sources were used (e.g. WHO, OECD, etc.)



## Price regulation in almost all PPRI member countries

### Role of EPR

EPR as main pricing policy: Canada, Israel, Kazakhstan  
EPR as supplementary pricing policy: Republic of Korea, South Africa  
No price regulation: Kyrgyzstan  
Austria: While EPR is as main pricing policy, it is a supplementary policy in the reimbursement process

- Price control at the ex-factory (or sometimes wholesale) price level in almost all PPRI member countries
- Mostly targeting reimbursable medicines or prescription-only medicines
- External price referencing is applied in 41 countries using different methodologies:
  - Country baskets ranges from 1 (Luxemburg) to 39 countries (Kazakhstan)
  - 18 of the EPR-applying PPRI countries employ an average or a median benchmark price, whereas 9 countries relate to the lowest price of the reference countries.
- 32 PPRI countries apply a so-called generic price link (i.e. the generic price is set at a defined percentage of the originator price), and 23 countries use this policy for biosimilar medicines.

### Use of HTA

Systematic use of HTA for some new medicines: Canada, Republic of Korea  
HTA components as part of pricing and reimbursement process for new medicines: Israel  
Work of HTA body not integrated in pricing and reimbursement process: Kazakhstan  
Plan to introduce HTA: South Africa  
No use of HTA: Kyrgyzstan

- Only one country with a full-fledged value-based pricing system: Sweden
- 37 apply HTA, or elements of HTA including pharmacoeconomic instruments in their pricing and/or reimbursement decisions, thereof 18 countries (e.g. Germany, France, Norway, UK) in a systematic way (with assessment and appraisal processes having been implemented).
- 32 countries with regulated wholesale remuneration and 43 countries with regulated pharmacy remuneration
- 23 countries apply tendering as the predominant procurement method for medicines used in hospitals.
- Managed-entry agreements (MEA) were reported from 33 PPRI network member countries. Financially-based MEA are more commonly used than performance-based MEA.

## In the majority of the PPRI countries a large share of pharmaceutical expenditure is covered by public payers

### Generic substitution

Mandatory generic substitution: South Africa  
Indicative generic substitution: Israel, Kazakhstan, Kyrgyzstan, Republic of Korea  
In Canada, generic substitution is mandatory in some provinces and indicative in other provinces

- 46 PPRI member countries have one or more reimbursement lists for outpatient medicines in place; of those 41 apply solely positive lists (i.e. explicitly indicating those medicines that are included in reimbursement).
- Key criteria for inclusion in coverage scheme: The (added) therapeutic benefit of a medicine, medical need, financial considerations such as budget impact and the cost-effectiveness
- 32 PPRI countries apply a reference price system (RPS), which defines the same reimbursement amount for similar or identical medicines in a cluster which are established at ATC-5 level in 18 countries and broader in the remaining.
- 43 PPRI countries have prescribing by international non-proprietary name in place and 43 countries implemented generic substitution. Biosimilar substitution, however, is only in place in 15 countries.

- At least 43 PPRI countries apply co-payments for outpatient reimbursable medicines, in the form of a prescription fee (20 countries), a percentage co-payment of the price of the medicine (30 countries) or a deductible (9 countries; some countries have more than one co-payment in place).
- All of these PPRI countries apply exemptions from or reductions of co-payments for defined population groups.

## Further research on impact on access to medicines needed

Since the implementation of pricing and reimbursement policies is in the national competence of governments, policies used vary greatly with regard to their aims, design and enforcement. For identifying best-practice policies with regard to facilitating affordable and equitable access to essential and cost-effective medicines further research is needed. This policy review offers descriptive information as basis for further research.

