



# Summer School Pharmaceutical Pricing and Reimbursement Policies

Monday, 23 July 2018 - Friday, 27 July 2018  
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**READER**

**Organiser:**

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WHO Collaborating Centre for Pharmaceutical Pricing and Reimbursement Policies, Department of Pharmacoeconomics at the Austrian Public Health Institute (Gesundheit Österreich GmbH)

in collaboration with the

World Health Organization, Regional Office for Europe

# About this reader

'Knowledge is power!' This reader provides references to key materials (e.g. studies, book chapters, articles, reports) in the field of pricing and reimbursement of medicines.

We prepared this reader to offer the participants of the Summer School a handy work of reference. This reader aims to minimise the information search costs for participants by presenting key documents. The studies selected have a focus on the European region. In principle, we considered more recent publications, but in some cases we also included flagship reports of the last decade given their importance.

In this printed version of the reader, you will be **provided selected parts** (e.g. Executive Summaries, abstracts, excerpts) of the larger materials. We will also share the full texts with the participants of the Summer School electronically (via download link). Links to the documents, if publicly accessible, are also offered.

The materials were classified to different chapters. Please note that some documents may address two or three sections – this is indicated in the list below.

While this reader aims to cover key documents, we had to be selective in its preparation, and as a result, it is not comprehensive.

## How to read the Reader

Continuous numbering of the documents

1.2 Frameworks for measuring access to medicines					
Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">Equitable access to essential medicines. a framework for collective action</a>	World Health Organization	2004	A key framework of four dimensions	02	1
<a href="#">Access to medicines from a health system perspective</a>	Bigdeli M, Jacobs B, Tomson G, Laing R, Ghaffar A, Dujardin B, et al.	2012	Article published in: Health policy and planning	03	-

Electronic link to the full version of the report/article

If the full text is not available via link, please consult the download area of the summer school:

<https://dory.goeg.at/s/JdgXSDoE24sB9fk>

PW: WHOCCsummer2018

For the documents we considered most important (in red letters), we included the executive summary/abstract in this Reader. You may find them on the indicated pages.

## Feedback

The selection of the documents was compiled by staff members of the Vienna WHO Collaborating Centre on Pharmaceutical Pricing and Reimbursement Policies. We would highly appreciate any comments on the reader: do you consider it as useful, do you miss any topics or documents, etc. We are pleased to receive your comments – please email to: [whocc@goeg.at](mailto:whocc@goeg.at).

*Enjoy reading!*



# Overview

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## 1. Theoretical / Methodological frameworks

### 1.1 Terminology

Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">Glossary of pharmaceutical terms. Update 2016</a> Online search: <a href="http://whocc.goeg.at/Glossary/Search">http://whocc.goeg.at/Glossary/Search</a>	WHO Collaborating Centre for Pharmaceutical pricing and Reimbursement Policies	2016	A updated glossary providing more than 400 terms of pharmaceutical pricing and reimbursement  Translations into German and Spanish are also available	01	–

### 1.2 Frameworks for measuring access to medicines

Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">Access to medicines from a health system perspective</a>	Bigdeli M, Jacobs B, Tomson G, Laing R, Ghaffar A, Dujardin B, et al.	2012	Article published in: Health policy and planning	02	–
<a href="#">Equitable access to essential medicines: a framework for collective action</a>	World Health Organization	2004	A key framework of four dimensions	03	1

### 1.3 Indicators

Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">PHIS Indicators. Taxonomy</a>	Lopes S, Zimmermann N, Vogler S	2009	A taxonomy for defining indicators of pharmaceutical pricing and reimbursement	04	–
<a href="#">Indicators for monitoring national drug policies. A practical manual</a>	World Health Organization	1999	A practical guide which data are required for steering the system	05	–

### 1.4 Pharmaceutical policy analysis and implementation

Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">Introduction to drug utilization research. Drug Utilization Research: Methods and Applications</a>	Wettermark B, Elseviers M, Almarsdóttir AB, Andersen M, Benko R, Bennie M, et al	2016	Book published at Wiley	06	–
<a href="#">Medicines in health systems: advancing access, affordability appropriate use</a>	Alliance for Health Policy and Systems Research & WHO	2014	An analysis of the medicines situation across low- and middle-income countries (outside Europe), offering tools for pharmaceutical policy advice	07	–
<a href="#">A practical approach to pharmaceutical policy</a>	Seiter A.	2010	A book of a World Bank experts about tools to analyse and implement pharmaceutical policy (focus on low- and middle-income countries)	08	–

<a href="#">How to develop and implement a national drug policy</a>	World Health Organization	2001	A guidance document	09	–
<a href="#">A Plan, Do, Check, Act framework</a> A description at the website of the Health and Safety Executive (UK)	–	–	A generally known tool	10	–

### 1.5 Essential Medicines List

Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">The selection and use of essential medicines. Report of the WHO Expert Committee, 2017</a>	World Health Organization	2017	Meeting report of the 20th Expert Committee meeting, 20–24 April 2015 in Geneva, in order to revise and update the WHO Model List of Essential Medicines (EML) for both adults and children	11	–
<a href="#">Essential medicines for cancer: WHO recommendations and national priorities</a>	Jane Robertson et al.	2016	Article in the Bulletin of the World Health Organization	12	–
<a href="#">The concept of essential medicines: lessons for rich countries</a>	Hogerzeil HV	2004	Article in the British Medical Journal	13	–
<a href="#">Twenty-five years of essential medicines</a>	Quick JD, Hogerzeil HV, Velásquez G, Rågo L	2002	Article in the Bulletin of the World Health Organization	14	–

### 2 Health / Universal Health Coverage and pharmaceutical expenditure and funding

Title	Authors	Year	Journal/Book/Comment	No.	Page
Financial protection in high-income countries. A comparison of the Czech Republic, Estonia and Latvia	Thomson S, Evetovits T, Cylus J	2018	Report of World Health Organization Regional Office for Europe	15	–
<a href="#">Baseline assessment of WHO's target for both availability and affordability of essential medicines to treat non-communicable diseases.</a>	Ewen M, Zweekhorst M, Regeer B, Laing R	2017	<a href="#">Plos One</a>	16	2
<a href="#">Drivers of expenditure on primary care prescription drugs in 10 high-income countries with universal health coverage</a>	Morgan SG, Leopold C, Wagner AK	2017	Canadian Medical Association Journal	17	–
<a href="#">Health care coverage in OECD countries in 2012</a>	Paris V, Hewlett E, Aaraaen A, Alexa J, Simon L	2016	<a href="#">OECD iLibrary</a>	18	3
<a href="#">Measurement of drug expenditure</a> Not publicly accessible	Vogler S, Martikainen J	2016	Book chapter in: Elsevier M, Wettermark B et al. Drug Utilization Research: Methods and Applications	19	–
<a href="#">Pharmaceutical Expenditure And Policies. Past Trends And Future Challenges</a>	Belloni A, Morgan D, Paris V	2016	An OECD Working Paper	20	–
<a href="#">The world medicines situation 2011. Medicine expenditures.</a>	Lu Y, Hernandez P, Abegunde D, Edejer T	2011	A chapter in the WHO World Medicines Situation report	21	–
<a href="#">Review 2: The Role of Health Insurance in the Cost-effective Use of Medicines</a>	WHO/HAI	2011	WHO/HAI review about role of health insurance (public funding) to improve cost-effective use of medicines	22	–

### 3 Country pharmaceutical policies and systems

#### 3.1 Country examples

Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">Short PPRI Pharma Profile Austria 2017</a>	Zimmermann N, Rainer L	2018	Gesundheit Österreich GmbH	23	–
<a href="#">An antibiotic's journey from marketing authorization to use, Norway.</a>	Årdal C, Blix HS, Plahte J, Røttingen J- A	2017	Bulletin of the World Health Organization	24	–
<a href="#">Pharmaceutical pricing and reimbursement reform in Kyrgyzstan</a>	Schneider P, Vogler S	2016	Report about improvements in the Kyrgyz pharmaceutical system	25	–
<a href="#">Availability of medicines in Estonia: an analysis of existing barriers and options to address them</a>	Ferrario A, Reinap M, Pedersen H.B, Kanavos P	2016	Analysis of Estonian pharmaceutical system with special focus on availability issues	26	–
<a href="#">Improving Access to Essential Medicines in the Republic of Moldova</a>	Bezverhni Z, Safta V, Chitan E, Ferrario A, Habicht J	2016	Article in Eurohealth	27	–
<a href="#">Improved Effectiveness of Generic Medicines Markets in Hungary</a>	Németh G, Szigeti S, Pusztai Z	2015	Report about generic policies in Hungary	28	–
<a href="#">Transitioning to a national health system in Cyprus: a stakeholder analysis of pharmaceutical policy reform</a>	Wouters OJ, Kanavos P.G	2015	Article about Cypriot system in WHO Bulletin	29	–
<a href="#">Short PPRI / PHIS Pharma Profile Austria 2013</a>	Vogler S, Schmickl B, Zimmermann N	2013	Country report about the Austrian pharmaceutical system	30	–
<a href="#">Pharmaceutical Policies in Finland. Challenges and opportunities</a>	Mossialos E, Srivastava D	2008	Analytical country report about Finland	31	–

#### 3.2 Cross-country comparison and overview of policies

Title	Authors	Year	Journal/Book/Comment	No.	Page
Medicines reimbursement policies in Europe	Vogler S, Haasis MA, Dede G, Lam J, Bak Pedersen H.	2018	Report (in print)	32	–
Ensuring access to medicines: How to redesign pricing, reimbursement and procurement?	Vogler S, Paris V, Panteli D.	2018	Policy Brief of the European Observatory on Health Systems and Policies (in print)	33	–
<a href="#">How Can Pricing and Reimbursement Policies Improve Affordable Access to Medicines? Lessons Learned from European Countries</a>	Vogler S, Paris V, Ferrario A, Wirtz VJ, de Joncheere K, Schneider P, et al	2017	Article in Applied Health Economics and Health Policy	34	–
<a href="#">Pharmaceutical regulation in 15 European countries</a>	Panteli D, Arickx F, Cleemput I, Dedet G, Eckhardt H, Fogarty E, et al	2016	Study that investigates a broad range of regulatory measures, spanning marketing authorization to generic substitution and resulting price levels in a sample of 16 European health systems	35	4
<a href="#">Policy interventions related to medicines: Survey of measures taken in European countries during 2010–2015</a> Link to abstract, full version – see Summer School download area	Vogler S, Zimmermann N, de Joncheere K	2016	Article in Health Policy	36	–

<a href="#">Pharmaceutical policies in a crisis? Challenges and solutions identified at the PPRI Conference</a>	Vogler S, Zimmermann N, Ferrario A, Wirtz V, de Joncheere K, Bak Pedersen H, Dedet G, Paris V, Mantel-Teeuwisse A, Babar Z-U-D and on behalf of the Scientific Programme Committee	2016	Article in Journal of Pharmaceutical Policy and Practice; key messages of the PPRI Conference	37	-
<a href="#">Postmarket policy considerations for biosimilar oncology drugs</a> <a href="#">Link to abstract, full version not available</a>	Renwick MJ, Smolina K, Gladstone EJ, Weymann D, Morgan SG	2016	Article in The Lancet Oncology	38	-
<a href="#">Access to Orphan Drugs: A Comprehensive Review of Legislations, Regulations and Policies in 35 Countries</a>	Gammie T, Lu CY, Babar ZU-D	2015	Plos one	39	-
<a href="#">From market access to patient access: overview of evidence-based approaches for the reimbursement and pricing of pharmaceuticals in 36 European countries</a>	<a href="#">Panteli D, Eckhardt H, Nolting A, Busse R, Kulig M</a>	<a href="#">2015</a>	<a href="#">Health Research Policy and Systems</a>	40	-
<a href="#">Access to new medicines in Europe: technical review of policy initiatives and opportunities for collaboration and research</a>	World Health Organization, Regional Office for Europe	2015	A stock-taking of different approaches in European countries to deal with high-priced medicines	41	6
<a href="#">Pharmaceutical Pricing in Europe.</a> Link to abstract, full version – see Summer School download area	Vogler S, Martikainen J.E	2015	Book Chapter in: Pharmaceutical Prices in the 21st Century. Informs about current pricing policies in European countries	42	-
<a href="#">Inequalities in medicine use in Central Eastern Europe: an empirical investigation of socioeconomic determinants in eight countries</a>	Vogler S, Österle A, Mayer S	2015	Article published in In: International Journal for Equity in Health; investigation of social inequalities in medicine use in 8 Central and Eastern European countries and their pharmaceutical policies as 2006–2008	43	-
<a href="#">WHO Guideline on Country Pharmaceutical Pricing Policies</a>	World Health Organization	2015	A WHO Guideline addressing several area of medicine prices (e.g. external price referencing, mark-up regulation, generics). Also provides evidence about existence and impact of policies	44	11
<a href="#">Study of the policy mix for the reimbursement of medicinal products. Proposal for a best practice-based approach based on stakeholder assessment</a>	Vogler S, Zimmermann N Habimana K	2014	Report for the European Commission, identifying priorities for policy objectives and preferences of policy measures of European stakeholders	45	-
<a href="#">Priority Medicine Report. Background Paper 8.3. Pricing and Reimbursement Policies: Impacts on Innovation</a>	Bouvy J, Vogler S	2013	Book chapter in the Priority medicines for Europe and the world – 2013 update report	46	14
<a href="#">Cost-containment policies in public pharmaceutical spending in the EU</a>	Carone G, Christoph Schwierz C, Xavier A	2012	Report of European Commission providing about pharmaceutical policies applied in EU Member States	47	18

<a href="#">Differences in costs of and access to pharmaceutical products in the EU</a>	Kanavos P, Vadoros S, Irwin R, Nicod E, Casson M	2011	Report for the European Parliament	48	21
<a href="#">Comparing pharmaceutical pricing and reimbursement policies in Croatia to the European Union Member States</a>	Vogler S, Habl C, Bogut M, Voncina L	2011	Article in Croatian Medical Journal, overview of pharmaceutical pricing and reimbursement in EU Member States	49	-
<a href="#">Pharmaceutical policies in European countries</a> Link to abstract, full version not available	Barros PP	2010	Literature overview of pharmaceutical policies	50	-
<a href="#">PHIS Hospital Pharma Report</a>	Vogler S, Habl C, Leopold C, Mazag J, Morak S, Zimmermann N	2010	Overview about pharmaceutical policies in hospital in European countries and hospital medicines price survey	51	-
<a href="#">PPRI Report</a>	Vogler S, Habl C, Leopold C, Rosian-Schikuta I, de Joncheere K, Lyager Thompsen T	2008	Report for the European Commission about pharmaceutical policies in European countries	52	-
<a href="#">Pharmaceutical Pricing Policies in a Global Market</a>	OECD	2008	OECD report about pricing policies in several countries	53	27
<a href="#">Analysis of differences and commonalities in pricing and reimbursement systems in Europe</a>	Espin J, Rovira J	2007	Report for the European Commission about 4 selected pharmaceutical policies	54	-

#### 4. Specific pharmaceutical and reimbursement policies

##### 4.1 External price referencing

Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">The End of the International Reference Pricing System?</a>	Persson U, Jönsson B	2016	Article published in Applied Health Economics and Health Policy	55	-
<a href="#">Study on enhanced cross-country coordination in the area of pharmaceutical product pricing</a>	Vogler S, Lepuschütz L, Schneider P, Stühlinger V	2015	Report about external price referencing and differencing policies, mapping exercise and options for improvement / implementation	56	39
<a href="#">Mapping External Reference Pricing Practices for Medicines.</a>	Espin J, Rovira J, Ewen M, Laing R.	2014	Health Action International and the Andalusian School of Public Health	57	-
<a href="#">External reference pricing of medicinal products: simulation-based considerations for cross-country coordination. Final</a>	Toumi M, Rémuzat C, Vataire A-L, Urbinati D.	2014	Report for European Commission	58	-
<a href="#">Pharmaceutical pricing: The use of external reference pricing</a>	Ruggeri K, Nolte E.	2013	Rand	59	-
<a href="#">Impact of External Price Referencing on Medicine Prices – A Price Comparison Among 14 European Countries</a>	Leopold C, Mantel-Teeuwiese AK, Seyfang L, Vogler S, de Joncheere K, Laing RO, Leufkens H	2012	Article about the impact of external price referencing in Southern Med Review	60	-

<a href="#">Differences in external price referencing in Europe – A descriptive overview.</a> Link to abstract, full version – see Summer School download area	Leopold C, Vogler S, Mantel–Teeuwisse A.K., De Joncheere K, Leufkens HGM, Laing R	2012	Article in Health Policy, mapping exercise in Europe	61	–
<a href="#">Review 1: External Reference Pricing &amp; Policy brief #1 Pharmaceutical Pricing Policies and Interventions</a>	WHO/HAI	2011 / 2014	WHO/HAI review about external price referencing worldwide: a mapping exercise and evidence about impact	62	44
<a href="#">Short– and Long–Term Effects of Value–Based Pricing vs. External Price Referencing</a>	Panos Kanavos, Elena Nicod, Jaime Espin and Stacey van den Aardweg	2010	Comparison of two policies	63	–
<a href="#">Impact of cross–reference pricing on pharmaceutical prices: manufacturers' pricing strategies and price regulation</a> Link to abstract, full version – see Summer School download area	Stargardt T, Schreyögg J	2006	Article published in Applied Health Economics and Health Policy	64	–
<a href="#">The impact of price regulation on the launch delay of new drugs—evidence from twenty–five major markets in the 1990s</a>	Danzon PM, Wang YR, Wang L.	2004	Article published in Health Economics, study of impact of parallel trade and external price referencing on launch delay	65	–

4.2 Value–based pricing					
Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">Value–Based Pricing: L'Enfant Terrible?</a>	Garner S, Rintoul A, Hill SR	2017	PharmacoEconomics	66	–
<a href="#">Value in Pharmaceutical Pricing</a>	Paris V, Belloni A	2013	OECD report about value–based pricing	67	49
<a href="#">Value based pricing for NHS drugs: an opportunity not to be missed?</a>	Claxton K, Briggs A, Buxton MJ, Culyer AJ, McCabe C, Walker S, et al.	2008	Article published in BMJ: British Medical Journal	68	–
<a href="#">Approach to valuation and pricing of future medicines</a>	Henry D, Lang D, Hill S	2004	Background paper to WHO Priority Medicines for Europe and the World “A Public Health Approach to Innovation”	69	–

See also Ref. No. 63 (Short– and Long–Term Effects of Value–Based Pricing vs. External Price Referencing)

4.3 Differential pricing					
Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">Value–Based Differential Pricing: Efficient Prices for Drugs in a Global Context</a> Link to abstract, full version – see Summer School download area	Danzon P, Towse A, Mestre–Ferrandiz J	2015	Article published in Health economics	70	–

<a href="#">European Union Pharmaceutical Markets: A Case for Differential Pricing?</a>	Towse A, Pistollato M, Mestre-Ferrandiz J, Khan Z, Kaura S, Garrison L	2015	Article published in International Journal of the Economics of Business, suggesting differential pricing for Europe	71	–
<a href="#">Differential pricing of pharmaceuticals: a bibliometric review of the literature</a> Link to abstract, full version – see Summer School download area	Babar ZUD, Atif M	2014	Article published in Journal of Pharmaceutical Health Services Research; global mapping; Wiley	72	–
<a href="#">Differential pricing of new pharmaceuticals in lower income European countries.</a> Link to abstract, full version – see Summer School download area	Kaló Z, Annemans L, Garrison LP.	2013	Article published in Expert review of pharmaco-economics & outcomes research	73	–
<a href="#">Differential pricing of pharmaceuticals: Review of current knowledge, new findings and ideas for action</a>	Yadav P.	2010	Report of the MIT Zaragoza International Logistics Program	74	52

See also Ref. No. 56 (Study on enhanced cross-country coordination in the area of pharmaceutical product pricing) and Ref. No. 63 (Short- and Long-Term Effects of Value-Based Pricing vs. External Price Referencing)

4.4 Tendering / Procurement					
Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">Tendering for off-patent outpatient medicines: lessons learned from experiences in Belgium, Denmark and the Netherlands</a>	Vogler S, Gombocz M, Zimmermann N	2017	Article in Journal of Pharmaceutical Health Services Research	75	–
<a href="#">How can voluntary cross-border collaboration in public procurement improve access to health technologies in Europe?</a>	Espín J, Rovira J, Calleja A, Azzopardi-Muscat N, Richardson E, Palm W, et al	2016	Policy Brief	76	–
<a href="#">Challenges and opportunities in improving access to medicines through efficient public procurement in WHO European Region</a>	Ferrario A, Kanavos P, Humbert T, Iwamoto K, Bak Pedersen H	2016	WHO report	77	55
<a href="#">Tendering for outpatient prescription pharmaceuticals: What can be learned from current practices in Europe?</a> Link to abstract, full version – see Summer School download area	Dylst P, Vulto A, Simoens S	2011	Article published in Health Policy; mapping exercise about tendering in the European out-patient sectors	78	–
<a href="#">Tender systems for outpatient pharmaceuticals in the European Union: Evidence from the Netherlands, Germany and Belgium</a>	Kanavos P, Seeley L, Vandoros S, Aardweg S	2009	EMINet report under the lead of LSE for the European Commission, Directorate-General Enterprise	79	–
<a href="#">Tendering of Pharmaceuticals in EU Member States and EEA countries. Results from the country survey</a>	Leopold C, Habl C, Vogler S	2008	Report for the Main Association of Austrian Social Health Insurance Institutions (HVB) on behalf of the European Social Insurance Platform (ESIP)	80	–

See also Ref No. 51 (PHIS Hospital Pharma Report)



4.5 Health Technology Assessment					
Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">Inception Impact Assessment – Strengthening of the EU cooperation on Health Technology Assessment (HTA)</a>	European Commission DG Sante	2016	Inception Impact Assessment by the European Commission	81	–
<a href="#">2015 Global Survey on Health Technology Assessment by National Authorities</a>	World Health Organization	2015	Worldwide mapping exercise of Health Technology Assessment and evidence-based decision making of public funding of health services	82	–
<a href="#">Review 6: Health Technology Assessment in Medicine Pricing and Reimbursement &amp; Policy brief #6 Pharmaceutical Pricing Policies and Interventions</a>	WHO/HAI	2013/2014	WHO/HAI review about HTA for medicines worldwide: a mapping exercise and evidence about impact	83	57
<a href="#">Reimbursement of pharmaceuticals: reference pricing versus health technology assessment</a>	Drummond M, Jönsson B, Rutten F, Stargardt T.	2011	Article published in The European Journal of Health Economics	84	–

4.6 Managed-entry agreements					
Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">Managed Entry Agreements for Pharmaceuticals in the Context of Adaptive Pathways in Europe</a>	Bouvy JC, Sapede C, Garner S	2018	Frontiers in Pharmacology	85	–
<a href="#">The Implementation of Managed Entry Agreements in Central and Eastern Europe: Findings and Implications.</a>	Ferrario A, Arāja D, Bochenek T, Čatić T, Dankó D, Dimitrova M, et al.	2017	PharmacoEconomics.	86	–
<a href="#">How to improve the Belgian process for Managed Entry Agreements? An analysis of the Belgian and international experience</a>	Belgian Health Care Knowledge Centre (KCE)	2017	Synthesis and the Report are of interest	87	–
<a href="#">Managed Entry Agreements for oncology drugs: lessons from the European experience to inform the future</a>	Pauwels K, Huys I, Vogler S, Casteels M, Simoens S	2017	Frontiers in Pharmacology	88	–
<a href="#">Dynamic outcomes based approaches to pricing and reimbursement of innovative medicines</a>	Lieven A, Luca P	2017	A Discussion Document	89	–
<a href="#">Dealing with uncertainty and high prices of new medicines: A comparative analysis of the use of managed entry agreements in Belgium, England, the Netherlands and Sweden</a> Link to abstract, full version – see Summer School download area	Ferrario A, Kanavos P	2015	Article published in Social Science Medicine	90	–
<a href="#">Managed entry agreements for pharmaceuticals: The European experience</a>	Ferrario A, Kanavos P	2013	Overview about managed entry agreements in Europe	91	62
<a href="#">Performance-based risk-sharing arrangements—good practices for design, implementation, and evaluation: report of the ISPOR good practices for performance-based risk-sharing arrangements task force.</a>	Garrison LP, Towse A, Briggs A, de Pourville G, Grueger J, Mohr PE, et al.	2013	Article published in Value in Health	92	–
<a href="#">Experiences and Impact of European Risk-Sharing Schemes Focusing on Oncology Medicines</a>	Jaime Espín, Joan Rovira and Leticia García	2011	Survey of managed entry agreements for oncology medicines	93	–
<a href="#">What principles should govern the use of managed entry agreements?</a>	Klemp M, Frønsdal K.B, Facey K	2011	Discussion paper	94	–

<a href="#">Risk sharing arrangements for pharmaceuticals: potential considerations and recommendations for European payers.</a>	Adamski J, Godman B, Ofierska-Sujkowska G, Osinska B, Herholz H, Wendykowska K, et al.	2010	Article published in BMC health services research	95	–
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4.7 Distribution remuneration and taxes					
Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">Review 3: The Regulation of Mark-ups in the Pharmaceutical Supply Chain &amp; Policy brief #3 Pharmaceutical Pricing Policies and Interventions</a>	WHO/HAI	2011 / 2014	WHO/HAI review about distribution remuneration worldwide: a mapping exercise and evidence about impact	96	66
<a href="#">Review 5: Sales Taxes on Medicines &amp; Policy brief #5 Pharmaceutical Pricing Policies and Interventions</a>	WHO/HAI	2011 / 2014	WHO/HAI review about taxes on medicines worldwide: a mapping exercise and evidence about impact	97	71
<a href="#">The Pharmaceutical Distribution Chain in the European Union: Structure and Impact on Pharmaceutical Prices</a>	Kanavos P, Schurer W, Vogler S	2011	An EMINet report for the European Commission	98	–
<a href="#">A comparative analysis of remuneration models for pharmaceutical professional services</a> Abstract; Full text not available	Bernsten C, Andersson K, Garipey Y, Simoens S	2010	Article in Health Policy, Overview of pharmacy remuneration	99	–

4.8 Generic and biosimilar pricing + uptake					
Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">Do pricing and usage-enhancing policies differ between biosimilars and generics? Findings from an international survey</a>	Vogler S, Schneider P	2017	Article in Generics and Biosimilars initiative Journal	100	–
<a href="#">Pricing and Reimbursement of Biosimilars in Central and Eastern European Countries</a>	Kawalec P, Stawowczyk E, Tesar T, Skoupa J, Turcu-Stiolica A, Dimitrova M, et al	2017	Article in Frontiers in Pharmacology	101	–
<a href="#">Biosimilars: How Can Payers Get Long-Term Savings?</a>	Mestre-Ferrandiz J, Towse A, Berdud M	2016	PharmacoEconomics	102	–
<a href="#">Sustainable Provision of Generic Medicines in Europe</a>	Simoens S	2013	Report of researcher at KU Leuven about generic policies across Europe	103	–
<a href="#">Demand-side policies to encourage the use of generic medicines: an overview</a> Link to abstract, full version – see Summer School download area	Dylst P, Vulto A, Simoens S	2013	Article in Expert Review of Pharmacoeconomics and Outcomes Research, discussion different policies for promoting generics	104	–
<a href="#">The impact of pharmaceutical pricing and reimbursement policies on generics uptake: implementation of policy options on generics in 29 European countries—an overview</a>	Vogler S	2012	Article published in In: Generics and Biosimilars Initiative Journal (GaBI Journal), providing an overview of major generic policies	105	–

<a href="#">Review 4: Competition Policy &amp; Policy brief #4 Pharmaceutical Pricing Policies and Interventions</a>	WHO/HAI	2011 / 2014	WHO/HAI review about competition policies (role of generics) worldwide: a mapping exercise and evidence about impact	106	77
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4.9 Internal price referencing					
Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">Reference pricing systems in Europe: characteristics and consequences</a>	Dylst P, Vulto A, Simoens S	2012	Article published in Generics Biosimilars Initiative Journal, providing an overview of reference price systems in Europe	107	–
<a href="#">Reference price systems in Europe</a>	Habl C, Vogler S, Leopold C, Schmickl B, Fröschl B	2008	Report (in German; executive summary in English; mapping about reference price systems in Europe, case studies and estimates on savings	108	–
<a href="#">The impact of generic reference pricing interventions in the statin market</a> <a href="#">Abstract; full text not available</a>	Puig-Junoy J.	2007	Article published in Health Policy	109	–
<a href="#">Pharmaceutical policies: effects of reference pricing, other pricing, and purchasing policies</a>	Aaserud M, Dahlgren A, Kosters J, Oxman A, Ramsay C, Sturm H.	2006	Report for Cochrane Database of Systematic Reviews	110	81

See also Ref. No. 84 (Reimbursement of pharmaceuticals: reference pricing versus health technology assessment)

4.10 Co-payments					
Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">Paying for Formerly Free Medicines in Spain After 1 Year of Co-Payment: Changes in the Number of Dispensed Prescriptions</a> <a href="#">Abstract</a>	Puig-Junoy J, Rodríguez-Feijó S, Lopez-Valcarcel BG	2014	Article published in Applied health economics and health policy	111	–
<a href="#">What impact do prescription drug charges have on efficiency and equity? Evidence from high-income countries</a>	Gemmill MC, Thomson S, Mossialos E.	2008	Article published in International Journal for Equity in Health	112	–

4.11 Horizon scanning					
Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">Horizon scanning for pharmaceuticals: proposal for the BeNeLuxA collaboration</a>	Belgian Health Care Knowledge Centre (KCE)	2017	Both the Synthesis and the Report are of interest	113	–
<a href="#">The Italian Horizon Scanning Project. – PubMed – NCBI</a> Link to abstract, full version – see Summer School download area	Joppi R, Demattè L, Menti AM, Pase D, Poggiani C, Mezzalira L.	2009	Article published in European journal of clinical pharmacology	114	–

5. Medicine prices					
5.1 Methodology and sources					
Title	Authors	Year	Journal/Book/Comment	No.	Page

<a href="#">International Medical Products Price Indicator Guide. 2015 Edition</a>	Management Sciences for Health (MSH), World Health Organisation (WHO)	2016	Guide to pharmaceutical and medical products prices on the international market	115	–
<a href="#">International drug price comparisons: quality assessment</a>	Machado M, O'Brodovich R, Krahn M, Einarson TR	2011	Revista Panamericana de Salud Publica	116	–
<a href="#">Measuring medicine prices, availability, affordability and price components</a>	WHO and Health Action International	2008	Second edition of manual for price survey	117	83
<a href="#">International price comparisons for pharmaceuticals</a> Link to abstract, full version – see Summer School download area	Danzon PM, Kim JD	1998	Article published in Pharmacoeconomics	118	–
<a href="#">Methodological aspects of international drug price comparisons</a> Link to abstract, full version – see Summer School download area	Andersson F	1993	Article in Pharmacoeconomics	119	–

5.2 Price studies					
5.2.1 Price studies focused on originator medicines					
Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">International price comparison of pharmaceuticals 2016 – a volume based analysis of Swedish pharmaceutical prices relative to 19 other European countries</a>	Aho E, Johansson P, Rönholm G	2017	Report by TLV Sweden, price analysis of 20 European countries	120	–
<a href="#">A comparative study of orphan drug prices in Europe</a>	Young KE, Soussi I, Hemels M, Toumi M	2017	Journal of Market Access & Health Policy	121	–
<a href="#">A price comparison of recently launched proprietary pharmaceuticals in the UK and the US</a>	Jørgensen J, Kefalas P	2016	Article in Journal of Market Access & Health Policy	122	–
<a href="#">Price comparison of high-cost medicines 2015. Brief report</a>	Vogler S, Schneider P, Zimmermann N	2016	Report by GÖG, price analysis of 28 European countries	123	–
<a href="#">Prices, Costs, and Affordability of New Medicines for Hepatitis C in 30 Countries: An Economic Analysis</a>	Iyengar S, Tay-Teo K, Vogler S, Beyer P, Wiktor S, De Joncheere K, Hill S	2016	Article published in PLoS Med., providing a global price survey for two Hepatitis C medicines	124	–
<a href="#">Cancer drugs in 16 European countries, Australia, and New Zealand: a cross-country price comparison study</a> Link to abstract, full version – see Summer School download area	Vogler S, Babar Z-U-D, Vitry A	2015	Article published in Lancet Oncology, providing a price survey of 31 originator medicines as of 2013	125	–
<a href="#">Analysis of Medicine Prices in New Zealand and 16 European Countries</a>	Vogler S, Kilpatrick K, Babar Z-U-D	2015	Article published in Value in Health, providing a price survey of 14 originator medicines as of 2012	126	–
<a href="#">Is Europe still heading to a common price level for on-patent medicines? An exploratory study among 15 Western European countries</a> Link to abstract, full version – see Summer School download area	Leopold C, Mantel-Teeuwisse AK, Vogler S, de Joncheere K, Laing RO, Leufkens HGM	2013	Article published in Health Policy, study a possible price convergence	127	–
<a href="#">Determinants of branded prescription medicine prices in OECD countries</a>  Link to abstract, full version – see Summer School download area	Kanavos PG, VANDOROS S	2011	Article published in Health Economics Policy and Law; investigation of determinants of the prices of branded prescription medicines in 15 OECD countries	128	91

<a href="#">Are Pharmaceuticals Still Inexpensive in Norway? A Comparison of Prescription Drug Prices in Ten European Countries</a>	Brekke KR, Holmås TH, Straume OR	2010 policy	Report comparing Norwegian prices to countries to which Norway references	129	–
<a href="#">Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis</a> Link to abstract, full version – see Summer School download area	Cameron A, Ewen M, Ross-Degnan D, Ball D, Laing R	2009	Article published in the <i>Lancet</i>	130	92
<a href="#">International prices and availability of pharmaceuticals in 2005</a>	Danzon PM, Furukawa MF	2008	Article published in <i>Health Affairs</i> , providing a price survey of the US with 11 other, mainly European countries, as of 2005	131	–

5.2.2 Price studies focused on generic medicines					
Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">A comparison of generic drug prices in seven European countries: a methodological analysis</a>	Wouters OJ, Kanavos PG	2017	BMC Health Services Research	132	–
<a href="#">How large are the differences between originator and generic prices? Analysis of five molecules in 16 European countries</a>	Vogler S	2013	Article published in <i>Farmeconomia Health economics and therapeutic pathways</i> , Supplement, looking at price differences between originator and generics	133	–
<a href="#">Switching from Originator Brand Medicines to Generic Equivalents in Selected Developing Countries: How Much Could Be Saved?</a>	Cameron A, Mantel-Teeuwisse AK, Leufkens HGM, Laing RO	2012	Article published in <i>Value in Health</i> . 2012;15(5):664–73	134	–
<a href="#">Does the Market Share of Generic Medicines Influence the Price Level?: A European Analysis</a>  Abstract; full text not available	Dylst P, Simoens S	2011	Article published in <i>PharmacoEconomics</i> , studying a possible relationship between generic market share and price level in European countries between 2002 and 2007	135	–
<a href="#">International comparison of generic medicine prices</a> Abstract; full text not available	Simoens S	2007	Article published in <i>Current Medical Research and Opinion</i>	136	–

5.2.3 Price studies in the hospital sector	
See Ref. No. 51 (PHIS Hospital Pharma Report), Ref. No. 139 (Discounts and Rebates Granted for Medicines for Hospital Use in Five European Countries)	

5.3 Discounts					
Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">Payers' experiences with confidential pharmaceutical price discounts: a survey of public and statutory health systems in North America, Europe, and Australasia</a>	Morgan S, Vogler S, Wagner AK	2017	Article in <i>Health Policy</i>	137	–
<a href="#">Actual costs of cancer drugs in 15 European countries</a> Link to abstract, full version – see Summer School download area	van Harten WH, Wind A, de Paoli P, Saghatchian M, Oberst S	2015	Article in <i>The Lancet Oncology</i>	138	–

<a href="#">Discounts and Rebates Granted for Medicines for Hospital Use in Five European Countries</a>	Vogler S, Zimmermann N, Leopold C, Habl C, Mazag J	2013	Article published in Open Pharmacoconomics & Health Economics Journal; providing information about differences between official list prices and discounted prices for 12 active ingredients in 25 hospitals in 5 European countries, as of 2009	139	–
<a href="#">The role of discounts and loss leaders in medicine procurement in Austrian hospitals – a primary survey of official and actual medicine prices</a>	Vogler S, Zimmermann N, Habl C, Mazag J	2013	Article published in In: Cost Effectiveness and Resource Allocation, providing information about official list prices and discounted prices for 12 active ingredients in 5 hospitals in Austria, as of 2009	140	–
<a href="#">International Best Practices For Negotiating 'Reimbursement Contracts' With Price Rebates From Pharmaceutical Companies</a>	Morgan S, Daw J, Thomson P.	2013	Article published in Health Affairs	141	–
<a href="#">Discounts and rebates granted to public payers for medicines in European countries</a>	Vogler S, Zimmermann N, Habl C, Piessnegger J, Bucsics A	2012	Article published in Southern Med Review, information about discounts and similar price-reducing arrangements in the out-patient and in-patient sectors of European countries	142	–

See also Ref No. 51 (PHIS Hospital Pharma Report)

## 6. Current challenges and issues for discussion

### 6.1 High prices and possible solutions

Title	Authors	Year	Journal/Book/Comment	No.	Page
Equitable Access to High-Cost Pharmaceuticals Full version – see Summer School download area	Babar Z–U–D	2018	Book with examples about countries' access to high-prices medicines and policies	143	–
<a href="#">The high price of anticancer drugs: origins, implications, barriers, solutions</a>	Prasad V, De Jesús K, Mailankody S	2017	Nature Reviews Clinical Oncology	144	–
<a href="#">Can Price Transparency Contribute to More Affordable Patient Access to Medicines?</a>	Vogler S, Paterson KR	2017	PharmacoEconomics – Open	145	–
<a href="#">Reimbursed Price of Orphan Drugs: Current Strategies and Potential Improvements</a>	Mincarone P, Leo CG, Sabina S, Sarriá-Santamera A, Taruscio D, Serrano-Aguilar PG, et al	2017	Public health genomics	146	–
<a href="#">New Health Technologies: Managing Access, Value and Sustainability</a>	OECD	2017	OECD analysis of policies affecting the use of pharmaceuticals, medical devices, precision medicine, and digital technology plus recommendations	147	93
<a href="#">Towards access 2030</a> This article is available free of charge, when logged in with a free account	Hill S, Kieny MP	2017	Article in The Lancet	148	–

<a href="#">Links between Pharmaceutical R&amp;D Models and Access to Affordable Medicines</a>	European Parliament; Directorate General For Internal Policies	2016	Study for the ENVI Committee, provides an overview of the main issues related to access to medicines in the EU and suggests options to policymakers to address the key challenges in order to improve access to medicines	149	–
The price of drugs	Wertheimer AI	2016	Article in Journal of Pharmaceutical Health Services Research	150	–
<a href="#">Essential medicines for universal health coverage</a> Link to abstract, full version – see Summer School download area	Wirtz VJ, Hogerzeil HV, Gray AL, Bigdeli M, de Joncheere CP, Ewen MA, et al	2016	The Lancet. This article is available free of charge, when logged in with a free account	151	96
<a href="#">Access to cancer medicines in Europe: An analysis of existing challenges and countries' responses</a>	Ferrario A	2016	A thesis submitted to the Department of Social Policy at the London School of Economics	152	–
<a href="#">Drug Regulation and Pricing — Can Regulators Influence Affordability?</a>	Eichler H-G, Hurts H, Broich K, Rasi G	2016	New England Journal of Medicine	153	100

## 6.2 Limited evidence about (added) benefits of medicines

Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">Availability of evidence of benefits on overall survival and quality of life of cancer drugs approved by European Medicines Agency: retrospective cohort study of drug approvals</a>	Davis C, Naci H, Gurpinar E, Poplavska E, Pinto A, Aggarwal A	2017	Bmj	154	–
<a href="#">How Much Is Life Worth: Cetuximab, Non-Small Cell Lung Cancer, and the \$440 Billion Question</a>	Fojo T, Grady C	2009	Journal of the National Cancer Institute	155	–

## 6.3 Shortages

Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">Drug shortages in European countries: a trade-off between market attractiveness and cost containment? BMC Health Services Research</a>	Pauwels K, Huys I, Casteels M, Simoens S	2014	Article published in BMC Health Services Research	156	–
<a href="#">Shortages of medicines: a complex global challenge</a>	Gray A, Manasse Jr HR	2012	Article about in Bulletin of the World Health Organization about causes for shortages globally	157	–
<a href="#">Drug shortages: a closer look at products, suppliers and volume volatility</a>	IMS Institute for Healthcare Informatics	2011	IMS Report about shortages world-wide	158	–

See also Ref No. 25 (Availability of medicines in Estonia: an analysis of existing barriers and options to address them), Ref. No. 64 (The impact of price regulation on the launch delay of new drugs—evidence from twenty-five major markets in the 1990s)

6.4 Costs of R+D, production costs and innovation					
Title	Authors	Year	Journal/Book/Comment	No.	Page
Ensuring access to medicines: How to stimulate innovation to meet real patients'needs?	Panteli D, Edwards S	2018	European Observatory o Health Systems and Policies (in print)	159	–
<a href="#">Propaganda or the cost of innovation?</a> Key messages; full text not available	Ghinea N, Lipworth W, Kerridge I	2016	Article published in BMJ	160	–
<a href="#">Betting on Hepatitis C: how financial speculation in drug development influences access to medicines</a> Key messages; full text not available	Roy V, King L	2016	Article published in BMJ	161	–
<a href="#">The \$2.6 billion pill—methodologic and policy considerations</a>	Avorn J.	2015	Comment published in New England Journal of Medicine	162	104
<a href="#">Minimum Costs for Producing Hepatitis C Direct-Acting Antivirals for Use in Large-Scale Treatment Access Programs in Developing Countries</a>	Hill A, Khoo S, Fortunak J, Simmons B, Ford N	2014	Article in Clinical Infectious Diseases	163	–
<a href="#">Demythologizing the high cost of pharmaceutical research.</a>	Light DW, Warburton RN	2011	Article published in Biosocieties	164	–

6.5 Patent issues					
Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">Private patents and public health</a>	T'Hoene E	2016	Report published by Health Action International	165	–
<a href="#">Promoting access to medical technologies and innovation</a>	World Trade Organization, WIPO, WHO	2012/2013	A report of 3 UN institutions about intersections between public health, intellectual property and trade	166	–
<a href="#">Intellectual property and pharmaceutical drugs: an ethical analysis</a> Abstract; full text not available	De George R	2005	Discussion paper	167	–

6.6 Financial crisis					
Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">Effect of the economic recession on pharmaceutical policy and medicine sales in eight European countries</a>	Leopold C, Mantel-Teeuwisse AK, Vogler S, Valkova S, de Joncheere K, Leufkens HG, et al.	2014	Article in Bulletin of the World Health Organization, investigation of pharmaceutical policy changes during the economic recession in eight European countries on sales and expenditure	168	–
<a href="#">Impact of pharmaceutical policy interventions on utilization of antipsychotic medicines in Finland and Portugal in times of economic recession: interrupted time series analyses</a>	Leopold C, Zhang F, Mantel-Teeuwisse A.K., Vogler S, Valkova S, Ross-Degnan D, Wagner A.K.	2014	Article published in International Journal for Equity in Health	169	–
<a href="#">Pharmaceutical policies in European countries in response to the global financial crisis</a>	Vogler S, Zimmermann N, Leopold C, de Joncheere K.	2011	Article published in Southern Med Review; study of policy measures as of 2010/2011 in response to the crisis	170	–



<a href="#">Impact of the economic recession on the pharmaceutical sector. 2010.</a>	Buysse I.	2010	Report of the WHO Collaborating Centre for Pharmacoepidemiology & Pharmaceutical Policy Analysis at Utrecht: Utrecht University about impact of recession about pharmaceutical expenditure and consumption	171	–
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## 6.7 Promotion

Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">Fact or Fiction? What Healthcare Professionals Need to Know about Pharmaceutical Marketing in the European Union</a>	Health Action International (HAI)	2016	Guide what healthcare professionals need to know about pharmaceutical marketing in the European Union	172	–

## 6.8 Efficient and responsible use

Title	Authors	Year	Journal/Book/Comment	No.	Page
Medication wasted–Contents and costs of medicines ending up in household garbage see Summer school download area	Vogler S, de Rooij RH	2018	Research in Social and Administrative Pharmacy	173	–
<a href="#">Tackling Wasteful Spending on Health</a>	OECD	2017	OECD report that systematically reviews strategies put in place by countries to limit ineffective spending and waste.	174	107

## 7. Regional cooperation

Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">Negotiating prices of drugs for rare diseases</a>	Henrarda S, Arickx F	2016	Bulletin of the WHO	175	–
<a href="#">Balancing Access to Medicines and Sustainability in Europe: an Analysis from the Network of Competent Authorities on Pricing and Reimbursement (CAPR)</a> <a href="#">Link to abstract, full version – see Summer School download area</a>	Pani L, Montilla S, Németh G, Russo P, Viceconte G, Vogler S	2016	Article published in Pharmacological Research	176	–
<a href="#">The Pharmaceutical Pricing and Reimbursement Information (PPRI) initiative–Experiences from engaging with pharmaceutical policy makers</a>	Vogler S, Leopold C, Zimmermann N, Habl C, de Joncheere K	2014	Article published in Health Policy and Technology, reporting about activities of the PPRI network	177	110
<a href="#">European network for Health Technology Assessment, EUnetHTA: Planning, development, and implementation of a sustainable European network for Health Technology Assessment</a>	Kristensen FB, Mäkelä M, Neikter SA, Rehnqvist N, Håheim LL, Mørland B, et al.	2009	Article published in International journal of technology assessment in health care	178	–

## 8. Policy documents: Reviews and plans

### 8.1 International

Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">Fair Pricing Forum. Informal Advisory Group Meeting</a>	World Health Organization	2017	WHO report of the proceedings of an informal WHO Advisory Group meeting on fair pricing which was held on 22–24 November 2016	179	–
<a href="#">Strengthening health systems for universal health coverage and sustainable development</a>	Kieny MP, Bekedam H, Dovlo D, Fitzgerald J, Habicht J, Harrison G, et al	2017	Bulletin of the WHO	180	–
<a href="#">Report of the United Nations Secretary General's High-Level Panel on Access to Medicines. Promoting innovation and access to health technologies</a>	United Nations Secretary General's High-Level Panel on Access to Medicines	2016	Final Report	181	111

### 8.2 Regional

Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">Innovative payment models for high-cost innovative medicines</a>	Expert Panel On Effective Ways Of Investing In Health	2018	Report of the Expert Panel of effective ways of investing in Health (EXPH)	182	115
<a href="#">Report on EU options for improving access to medicines</a>	European Parliament	2017	Report of the Committee on the Environment, Public Health and Food Safety	183	–
<a href="#">Summary of Medicines Plan</a>	Ministry of Health, Welfare and Sports, NL	2016	Report of the Dutch Presidency of the Council of the European Union	184	–
<a href="#">Tackling drug-resistant infections globally: Final Report and Recommendations</a>	O'Neill J	2016	Report of the Review on antimicrobial resistance	185	–
<a href="#">Council conclusions on strengthening the balance in the pharmaceutical systems in the EU and its Member States</a>	The Council of the European Union	2016	Conclusions of the European Council	186	–

See also Ref No. [How can voluntary cross-border collaboration in public procurement improve access to health technologies in Europe?](#) ( No. 76)

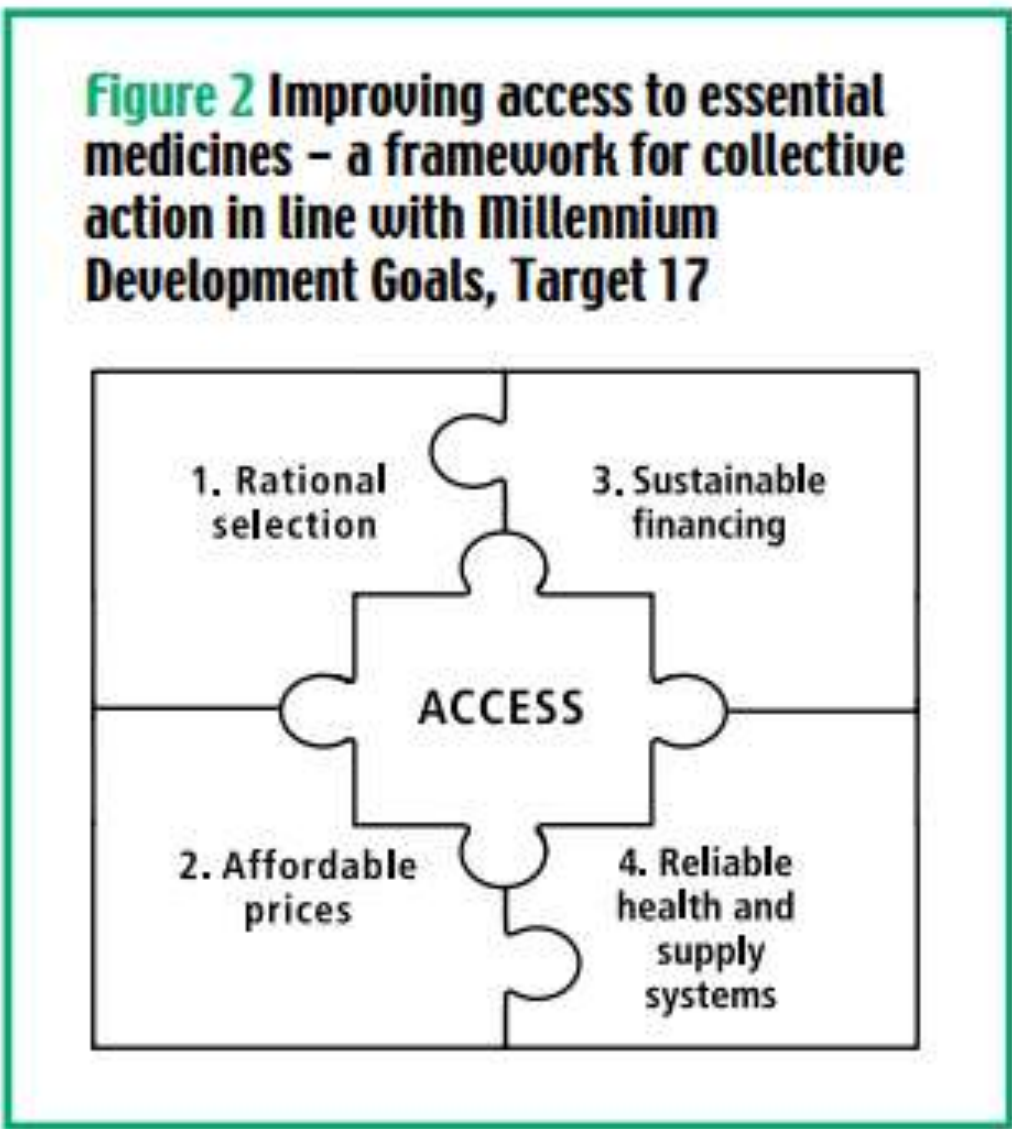
## 9. Clinical Reviews

Title	Authors	Year	Journal/Book/Comment	No.	Page
<a href="#">Interviews about ideas &amp; innovations in medicine, science &amp; clinical practice</a>	–	–	JAMA – Journal of the American Medical Association: Collection of interviews conducted between 2015 and 2018 on Podcast Republic website	187	–



# Equitable access to essential medicines: a framework for collective action

World Health Organization. 2004  
A key framework of four dimensions



# Baseline assessment of WHO's target for both availability and affordability of essential medicines to treat non-communicable diseases

Ewen M, Zweekhorst M, Regeer B, Laing R 2017

Plos One

## Abstract

### Background

WHO has set a voluntary target of 80% availability of affordable essential medicines, including generics, to treat major non-communicable diseases (NCDs), in the public and private sectors of countries by 2025. We undertook a secondary analysis of data from 30 surveys in low- and middle-income countries, conducted from 2008–2015 using the World Health Organization (WHO)/Health Action International (HAI) medicine availability and price survey methodology, to establish a baseline for this target.

### Methods

Data for 49 medicines (lowest priced generics and originator brands) to treat cardiovascular diseases (CVD), diabetes, chronic obstructive pulmonary diseases (COPD) and central nervous system (CNS) conditions were analysed to determine their availability in healthcare facilities and pharmacies, their affordability for those on low incomes (based on median patient prices of each medicine), and the percentage of medicines that were both available and affordable. Affordability was expressed as the number of days' wages of the lowest-paid unskilled government worker needed to purchase 30 days' supply using standard treatment regimens. Paying more than 1 days' wages was considered unaffordable.

### Findings

In low-income countries, 15.2% and 18.9% of lowest-priced generics met WHO's target in the public and private sectors, respectively, and 2.6% and 5.2% of originator brands. In lower-middle income countries, 23.8% and 23.2% of lowest priced generics, and 0.8% and 1.4% of originator brands, met the target in the public and private sectors, respectively. In upper-middle income countries, the situation was better for generics but still suboptimal as 36.0% and 39.4% met the target in public and private sectors, respectively. For originator brands in upper-middle income countries, none reached the target in the public sector and 13.7% in the private sector. Across the therapeutic groups for lowest priced generics, CVD medicines in low-income countries (11.9%), and CNS medicines in lower-middle (10.2%) and upper-middle income countries (33.3%), were least available and affordable in the public sector. In the private sector for lowest priced generics, CNS medicines were least available and affordable in all three country income groups (11.4%, 5.8% and 29.3% in low-, lower-middle and upper-middle income countries respectively).

### Interpretation

This data, which can act as a baseline for the WHO target, shows low availability and/or poor affordability is resulting in few essential NCD medicines meeting the target in low- and middle-income countries. In the era of Sustainable Development Goals, and as countries work to achieve Universal Health Coverage, increased commitments are needed by governments to improve the situation through the development of evidence-informed, nationally-contextualised interventions, with regular monitoring of NCD medicine availability, patient prices and affordability.

# Health care coverage in OECD countries in 2012

Paris V, Hewlett E, Auraaen A, Alexa J, Simon L. 2016

OECD iLibrary



18

## Abstract

This paper provides a detailed description of health coverage in OECD countries in 2012. It includes information on the organisation of health coverage (residence-based vs contributory systems), on the range of benefits covered by basic health coverage and on cost-sharing requirements. It also describes policies implemented to ensure universal health coverage –in most countries- and to limit user charges for vulnerable populations or people exposed to high health spending. The paper then describes the role played by voluntary health insurance as a secondary source of coverage. Combining qualitative information collected through a survey of OECD countries on benefits covered and cost-sharing requirements with spending data collected through the system of health accounts for 2012, this paper provides valuable information on health care coverage in OECD countries at a time universal health coverage is high on the policy agenda of many countries.

## Health care coverage in OECD countries in 2012

English

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Valérie Paris, Emily Hewlett<sup>1</sup>, Ane Auraaen<sup>1</sup>, Jan Alexa<sup>2</sup>, Lisa Simon<sup>1</sup>

<sup>1</sup>: OECD, France

<sup>2</sup>: Organization of American States, United States

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This paper provides a detailed description of health coverage in OECD countries in 2012. It includes information on the organisation of health coverage (residence-based vs contributory systems), on the range of benefits covered by basic health coverage and on cost-sharing requirements. It also describes policies implemented to ensure universal health coverage –in most countries- and to limit user charges for vulnerable populations or people exposed to high health spending. The paper then describes the role played by voluntary health insurance as a secondary source of coverage. Combining qualitative information collected through a survey of OECD countries on benefits covered and cost-sharing requirements with spending data collected through the system of health accounts for 2012, this paper provides valuable information on health care coverage in OECD countries at a time universal health coverage is high on the policy agenda of many countries.



## Executive summary

In the context of pharmaceutical care, policy-makers repeatedly face the challenge of balancing patient access to effective medicines with affordability and rising costs. The main goal of this study is to illustrate direct and indirect regulatory strategies shaping pharmaceutical care in different European countries in a systematic, comparative manner in the hopes of guiding the health policy discourse towards questions that are important to those covered in publicly financed (statutory) systems – and thus to actual and potential patients – particularly regarding quality of care.

The investigation spans measures related to marketing authorization; pricing and price updates; post-marketing evaluations guiding coverage decisions (health technology assessment); patient cost-sharing; specific cost and quality control measures targeting individual stakeholder groups (manufacturers, wholesalers/pharmacists, prescribers); generic substitution; and resulting price levels.

A sample of 16 European health systems was selected (Austria, Belgium, Denmark, England, Finland, France, Germany, Greece, Ireland, Italy, the Netherlands, Poland, Portugal, Scotland, Spain and Sweden). Quantitative data from the OECD and country-specific regulatory documents, as well as published and grey literature, were combined to form an initial evidence base in the form of health system profiles, which were then sent to relevant experts for review and validation.

All countries employ a mix of regulatory mechanisms to contain pharmaceutical expenditure and ensure quality and efficiency in pharmaceutical care, albeit with varying configurations and rigour. This variation also influences the extent of publicly financed pharmaceutical costs. Overall, observed differences in pharmaceutical expenditure should be interpreted in

conjunction with the differing volume and composition of consumption and price levels, as well as dispensation practices and their impact on measurement of pharmaceutical costs.

While for some countries timely and/or equitable access to new medicines may constitute a priority – or pose a substantial challenge – others may primarily be concerned with quality of care and containing public pharmaceutical expenditure. With the proliferation of specialty medicines and recent examples of high-cost pharmaceuticals with proven therapeutic benefit and substantial target populations, sustainability of financing in pharmaceutical care is another overarching concern to be addressed.

No definitive evidence has yet been produced on the effects of different cost-containment measures on patient outcomes. Depending on the foremost policy concerns in each country, different levers will have to be used to enable the delivery of appropriate care at affordable prices; monitoring of implemented regulation is vital to ensure that patient access and sustainability of financing are taken into account.



## Access to new medicines in Europe: technical review of policy initiatives and opportunities for collaboration and research

World Health Organization, Regional Office for Europe. 2015

A stock-taking of different approaches in European countries to deal with high-priced medicines

### Key messages

This report, with a focus on sustainable access to new medicines, reviews policies that affect medicines throughout their lifecycle (from research and development to disinvestment), examining the current evidence base across Europe. While many European countries have not traditionally required active priority-setting for access to medicines, appraising new medicines using pharmacoeconomics is increasingly seen as critical in order to improve efficiency in spending while maintaining an appropriate balance between access and cost-effectiveness. The following are the key messages to be drawn from the respective sections of the report.

### Current trends, practices and evidence of pharmaceutical consumption and use in Europe (section 2)

- The current rapid pace of therapeutic innovation, particularly for noncommunicable diseases (NCDs), is extremely positive from a patient perspective.
- At the same time, the introduction of these new products is adding both therapeutic complexity and higher costs, in turn putting increasing pressure on many European health systems.
- To mitigate such pressures and to balance the demand for new medicines and the financial impact of their introduction, further development of systems and processes to optimize the entry of new medicines is necessary across Europe; this applies both in countries with well developed medicine policies and regulation traditions and in those with less mature systems.
- Key steps in these processes should include methods to distinguish and reward meaningful clinical innovation, as well as evaluation mechanisms to assess the benefits in practice of the introduction of the medicines and impacts on health system budgets.

### Pre-launch activities – anticipating potential requirements and impact (section 3)

- Pre-launch activities for new medicines can systematically anticipate and prioritize therapeutic innovation with the highest potential for impact on clinical care, the health care system and patient outcomes, preparing the health system for swift access to such innovations. They also help to assess whether to instigate educational and other activities before the launch of a new medicine to enhance appropriate prescribing after the launch. As a result, pre-launch activities assist policy-makers in taking a longer-term strategic approach to the development of their health care systems and to considerations of access to interventions.
- Pre-launch activities assist with prescribing planning, demand assessment and budget estimation to assess the potential impact of new medicines and national guidance on the health economy. There are few public sector examples in the European context to date; however, those that exist show that strategic forecasting of projected use has had an impact on shaping the markets. Potential gains could be made in analysing and forecasting strategic product needs – a new European Union (EU) initiative is piloting this in relation to influenza vaccines and antiviral medicines.
- Transparent methods and systems for evaluating the therapeutic value of new medicines can improve evidence-informed decision-making and better inform the public of benefits and risks related to new treatments.
- Debate is ongoing about whether the regulatory approach to evidence-based medicines can change to adaptive licensing. For some product groups the first step in changing regulation has been taken and products are launched with conditional approval, with limited data on effectiveness and safety. New medicines licensing approaches require careful consideration, particularly in the context of the health systems of the different countries where regulatory decisions will be implemented. They may also require health authorities to be able to implement disinvestment strategies should the



new medicine be shown to have limited value in routine clinical care, since withdrawal of medicines is problematic.

- Adequate assessment of health gains of new medicines versus current treatment requires ongoing physician involvement and education in critical drug evaluation skills, as well as coordination of patient registries.
- Potential ways to expand the benefits from current pre-launch work include greater scrutiny in differentiating innovation and improvements presented by new products in a meaningful way in the context of different health care systems, continued collaboration by payers on standards and criteria for evaluation of benefits and cost–efficiency, transparency and open prioritization with engagement of stakeholders.

#### **Peri-launch activities – pricing and reimbursement methods for in-patient medicines (section 4)**

- European countries use a swathe of different methods to set their prices but most still rely on external reference pricing (ERP).
- Consensus is increasing among payers that medicines should be priced according to the added therapeutic value they deliver. Nevertheless, implementing such a value-based pricing (VBP) system is complicated by methodological challenges and data availability.
- Increasingly, countries are using health technology assessment (HTA) to guide their reimbursement decisions. This may be done in conjunction with budget impact analysis. Conducting HTA through multicriteria decision analysis (MCDA) has been proposed as a way to address some of the limitations of current HTA methods.
- Managed-entry agreements (MEAs), rebates, clawbacks and paybacks are widely used tools to generate savings without affecting list prices.
- Achieving fair pricing and ensuring long-term sustainability of health care systems and access for patients is one of the biggest challenges for health and pharmaceutical systems in Europe and worldwide. Industry supports differential pricing with price confidentiality and a modified ERP system to achieve this. Some stakeholders are concerned about price confidentiality; others think it is the only way to grant lower prices to less wealthy countries. Consensus on such issues is unlikely in the immediate future owing to competing stakeholder interests and certain peculiarities of the European pharmaceutical market (such as parallel trade, extensive use of ERP and large disparities between countries in ability to pay).

#### **Post-launch activities: guidelines, formularies and interface management (section 5)**

- All activities carried out to address the appropriate and sustainable use of medicines are principally centred on an evidence-based assessment of their risk–benefit profile.
- Clinical guidelines can promote the appropriate use of drugs, provided that their recommendations are explicit; weighted, following a transparent and systematic assessment of the available evidence; and implemented by clinicians.
- Implementation strategies tailored to local contexts and a shared approach with local practitioners should be developed to put recommendations into practice, mainly considering the configuration of health services, available resources and health professionals' skills and attitudes, along with relevant patient perspectives. This can include quality indicators, which should be developed from pre-launch onwards.
- Essential or “wise” medicines lists induce the use of the most effective and safest drugs and help consolidate prescribers' familiarity with them; more inclusive formularies can also define and prioritize the therapeutic context of drug use.
- In many European countries responsibility and funding for medicines used in the outpatient and inpatient sectors are split (for example, social health insurance funds outpatient medicines and medicines used in hospitals are financed from hospital budgets); this dual financing of pharmaceutical systems can incentivize a shift of treatments and patients between sectors.



- The need for improved medicines management at the interface of the outpatient and hospital sectors has increasingly been acknowledged.
- Activities to improve interface management may include initiatives at the micro level (such as hospital discharge programmes) and policies at the macro level (such as joint reimbursement lists and joint drug and therapeutics committees (DTCs)). The latter may include approaches that aim to overcome the challenge of dual funding.

## **Impact of policies on funding and use of new drugs – some examples (section 6)**

### ***New medicines for patients with cancer***

- Cancer is one of the most important NCDs. Costs, including the costs of new cancer medicines, however, are rising at an unsustainable rate, threatening continued access to cancer care and other priorities.
- Prices of new cancer drugs have doubled during the past 10 years and are now typically between US\$ 6000 and US\$ 10 000 per month, often with little relationship between reimbursed costs and associated health benefits.
- Debate is ongoing about whether differences in spend among countries on cancer care actually translate into improved patient outcomes. Key factors affecting differences in outcomes include issues such as lifestyle, late diagnosis and management approaches, particularly for patients aged 65 and over.
- Differences exist in the use of new cancer medicines across Europe: reasons include differences in reimbursement and funding, as well as access to specialist services.
- Potential ways to address these issues include greater scrutiny regarding the costs and cost-effectiveness of new cancer medicines, including agreement on the definition of “meaningful clinical benefits” for given tumours.

### ***Access to tumour necrosis factor (TNF) alpha inhibitors in Europe***

- The introduction of TNF alpha inhibitors in the late 1990s represented a breakthrough in the treatment of diseases such as rheumatoid arthritis but, despite their disease-modifying effects, widespread use has been hindered by their relatively high cost and adverse side-effects, leading to reimbursement or usage restrictions in most European countries.
- Substantial variations exist in national guidelines for the treatment of rheumatoid arthritis across Europe.
- Differences in access occur, resulting from variations in availability of rheumatologists and time from symptoms to diagnosis or treatment. Further disparities in access to TNF inhibitors for rheumatoid arthritis patients are associated with countries’ socioeconomic development and co-payment levels. The difference in affordability between western Europe and the new EU Member States is explained by the relationships among gross domestic product (GDP), expenditure on health and global drug prices.
- The introduction of biosimilar medicines may reduce costs and increase access to biological products, but experiences with biosimilars are still new. Further experience and evidence of the substitution of biological therapy in practice is required to assess risk and harms.

### ***New therapeutics for hepatitis C***

- Access to new innovative medicines and diagnostics is an important element for the control and treatment of hepatitis C infection.
- The prices requested for the new hepatitis C medicines – in particular the direct-acting antivirals as sofosbuvir – are unsustainable for most countries’ health budgets. These prices may preclude thousands of patients from benefiting from a curative treatment that might therefore remain accessible only to the most severely ill patients – in many countries they are restricted to hepatic fibrosis F3A4 and early stages are not treated; hence, this transmissible disease will continue to drive new infections.



- Access in high-income countries, like the EU Member States, to innovative treatment products such as anti-infective medicines could be revisited using a new tool – the European Commission (EC) Joint Procurement Agreement – which sets out the modalities under which EU countries can jointly procure medical products.
- Understanding and addressing current challenges regarding hepatitis C medicine are important for the future introduction of new medicines in other areas. With a focus on public health, a dialogue with stakeholders on access to innovation is urgently required.
- Closer collaboration between countries in Europe can foster new achievements. This may be linked, for example, to potential definition of price ceilings, joint or pooled procurement, standard treatment protocols and guidelines, and collaboration on patient registries.

### ***New orphan drugs***

- New orphan medicinal products (OMPs) are a challenge to health authorities, in view of the large number of orphan disease areas where there is still unmet need, coupled with the considerable and growing prices requested per patient, which typically exceed average annual acquisition costs of US\$ 200 000–500 000 per patient per year.
- Incentives have been offered for pharmaceutical manufacturers to research and develop new OMPs to address identified areas of unmet need. Growing pressure on available resources, as well as some orphan drugs achieving “blockbuster” status (the term for drugs that earn the manufacturer over US\$ 1 billion per year in sales), however, means that this practice is now being challenged. This has resulted in some OMPs being denied reimbursement, a growth in MEAs for OMPs to enhance their value and the development of new approaches to valuing orphan drugs, including MCDA tools.
- As no universally accepted metric exists on what currently constitutes a high price for a new OMP or new drug seeking orphan disease status, the use of approaches such as MCDA tools among authorities across Europe will grow. This is mindful of the need to continue to stimulate research into new OMPs to treat rare and high-priority disease areas, to address continuing considerable unmet need balanced against considerable pressure on available resources. In the first instance these resource pressures are likely to lead to more restrictive criteria for granting premium prices for new OMPs and the growth in pan-European patient registries to improve the evidence base. Subsequently, developing more uniform criteria across Europe for valuing new OMPs will be needed.

### ***New drugs for patients with type 2 diabetes***

- Type 2 diabetes is a global public health challenge: it is projected that in 2035 over 1 billion people will be affected by or at risk of the disease.
- Nonpharmacological approaches comprising intensive lifestyle interventions – including healthy diet, regular physical activity and avoidance of tobacco and alcohol use – have been shown to prevent or delay the onset of type 2 diabetes and to improve health outcomes in patients who have already developed the disease.
- Lifestyle management and metformin are effective and affordable interventions that can reduce the economic burden of diabetes and reduce mortality. Interventions to improve adherence to these treatment options are required.
- Insufficient evidence is currently available to recommend the most effective medicine to augment therapy once the disease can no longer be controlled with metformin alone. As the disease progresses, initiation of insulin treatment is recommended. Comparative effectiveness and safety research into new therapies is needed to justify the choice of treatment regimens.
- The cost-effectiveness of the available treatment options should be considered when selecting glucose-lowering agents. Less expensive agents should be chosen in resource-poor settings.

### Future directions and brief conclusions (section 7)

- Decision-makers are increasingly faced with difficult choices and are required to make informed decisions. This involves greater use of information technology (IT), better steering of medical practitioners to comply with clinical evidence (perhaps through a combination of financial and nonfinancial incentives) and better targeting of national drug policies to those using resources more intensely (multicomorbidity patterns).
- Prioritization processes will increasingly be required for introduction of new medicines and should incorporate principles of collaboration and transparency.
- Cooperation between countries in Europe and stakeholder dialogues on what constitutes a fair reward for industry innovation while still preserving access for patients could be further strengthened. Cooperation between stakeholders should involve better balancing of the value of innovation with equitable, affordable patient access.
- Collaboration among regional or subregional health systems might benefit from including a particular focus on chronic care, specialty medicines and rare diseases.

## **WHO Guideline on Country Pharmaceutical Pricing Policies**

World Health Organization 2013.

A WHO Guideline addressing several area of medicine prices (e.g. external price referencing, mark-up regulation, generics). Also provides evidence about existence and impact of policies.

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## Box 1: Guideline recommendations and key principles

POLICY INTERVENTION	RECOMMENDATIONS
<b>Regulation of mark-ups in the pharmaceutical supply and distribution chain</b>	<ul style="list-style-type: none"> <li>➤ As part of an overall pharmaceutical pricing strategy, countries should consider regulating distribution chain mark-ups (distributors/wholesalers).</li> <li>➤ As part of an overall pharmaceutical pricing strategy, countries should consider regulating retail chain mark-ups and fees (pharmacies, dispensing doctors, dispensaries).</li> <li>➤ If mark-ups are regulated, countries should consider using regressive mark-ups (lower mark-up for higher-priced products) rather than fixed percentage mark-ups, given the incentive that the latter provides for higher-priced products to receive a higher net margin.</li> <li>➤ Countries should consider using remuneration/mark-up regulation to provide incentives for supplying specific medicines (generics, low volume medicines, reimbursable medicines) or to protect specific patients or population groups (e.g., vulnerable groups, remote populations).</li> <li>➤ In systems where rebates and discounts in the distribution chain occur, countries should consider regulating them and should make them transparent. The information should be taken into account when reviewing and regulating mark-ups and prices.</li> </ul>
<b>Tax exemptions/reductions for pharmaceutical products</b>	<ul style="list-style-type: none"> <li>➤ Countries should consider exempting essential medicines from taxation.</li> <li>➤ Countries should ensure any tax reductions or exemptions result in lowered prices to the patient/purchaser.</li> </ul>
<b>Application of cost-plus pricing formulae for pharmaceutical price setting</b>	<ul style="list-style-type: none"> <li>➤ Countries generally should not use cost-plus as an overall pharmaceutical pricing policy.</li> <li>➤ Countries using a cost-plus method as an overall policy that wish to change their strategy should consider replacing or complementing the cost-plus approach with other policies, including those covered in this guideline.</li> </ul>
<b>Use of external reference pricing</b>	<ul style="list-style-type: none"> <li>➤ Countries should consider using external reference pricing as a method for negotiating or benchmarking the price of a medicine.</li> <li>➤ Countries should consider using external reference pricing as part of an overall strategy, in combination with other methods, for setting the price of a medicine.</li> <li>➤ In developing an external reference pricing system, countries should define transparent methods and processes to be used.</li> <li>➤ Countries /payers should select comparator countries to use for ERP based on economic status, pharmaceutical pricing systems in place, the publication of actual versus negotiated or concealed prices, exact comparator products supplied, and similar burden of disease.</li> </ul>
<b>Promotion of use of generic medicines</b>	<ul style="list-style-type: none"> <li>➤ Countries should enable the early market entry of generics through legislative and administrative measures that encourage early submission of regulatory applications, and allow for prompt and effective review.</li> <li>➤ Countries should use multiple strategies to achieve low priced generics, depending on the system and market. These strategies may include: within-country reference pricing, tendering, and/or lower co-payments.</li> <li>➤ In order to maximize uptake of generics, countries should implement (and enforce as appropriate) a mix of policies and strategies, including:             <ul style="list-style-type: none"> <li>○ Legislation to allow generic substitution by dispensers;</li> <li>○ Legislative structure and incentives for prescribers to prescribe by international nonproprietary name;</li> <li>○ Dispensing fees that encourage use of low price generics;</li> <li>○ Regressive margins and incentives for dispensers; and</li> <li>○ Consumer and professional education regarding quality and price of generics.</li> </ul> </li> </ul>



POLICY INTERVENTION	RECOMMENDATIONS
<p><b>Use of health technology assessment</b></p>	<ul style="list-style-type: none"> <li>➤ Countries should use health technology assessment (HTA) as a tool to support reimbursement decision-making as well as price setting/negotiation.</li> <li>➤ Countries should combine HTA with other policies and strategies, particularly within-country reference pricing (by chemical entity, pharmacological class, or indication).</li> <li>➤ Countries should consider the following approaches for using HTA: review of applicability and adaptation of reports from other countries; review of reports submitted by pharmaceutical companies; conduct assessments based on local information and local data. The choice of approach depends on technical capacity and local decision-making structures.</li> <li>➤ Countries could take a stepwise approach to develop legislative and technical capacity to take full advantage of the potential utility of HTA in pharmaceutical price setting.</li> <li>➤ In establishing the legislative/administrative framework, countries should clearly define the roles and responsibilities of the decision-makers and other stakeholders, and the process of decision-making.</li> <li>➤ Countries should ensure that HTA processes are transparent and that the assessment reports and decisions should be made publicly available and effectively disseminated to stakeholders.</li> <li>➤ Countries should collaborate to promote exchange of information and develop common requirements for HTA.</li> </ul>
<p><b>KEY PRINCIPLES</b></p>	
<ul style="list-style-type: none"> <li>• Countries should use a combination of different pharmaceutical pricing policies that should be selected based on the objective, context and health system.</li> <li>• Countries should make their pricing policies, processes, and decisions transparent.</li> <li>• Pricing policies should have an appropriate legislative framework and governance and administrative structures, supported by technical capacity, and should be regularly reviewed, monitored (including actual prices) and evaluated and amended as necessary.</li> <li>• In promoting the use of affordable medicines, countries should employ a combination of pharmaceutical policies that address both supply and demand issues.</li> <li>• If regulation of pharmaceutical prices is introduced, effective implementation will be required to ensure compliance (e.g. incentives, enforcement, price monitoring system, fines).</li> <li>• Countries should adopt policies to promote the use of quality assured generic medicines in order to increase access and affordability.</li> <li>• Countries should collaborate to promote exchange of information about policies, their impacts, and pharmaceutical prices.</li> </ul>	

In developing the recommendations, the panel noted that the overall quality of research and evidence in relation to pharmaceutical policy implementation and impact is poor, especially in developing country settings. There are many areas where more descriptive studies and good quality research would allow better understanding of what policies should be chosen and how they should be implemented. However, it is clear that such research takes time to complete and therefore the panel recommended that the guideline should be reviewed for potential update in 5 years.



## Priority Medicine Report. Background Paper 8.3. Pricing and Reimbursement Policies: Impacts on Innovation

Bouvy J, Vogler S. 2013

Book chapter in the Priority medicines for Europe and the world – 2013 update report

### 5. Conclusions

This background paper started with the notion that one of the major challenges in (inter)national policies regarding the pricing and reimbursement of medicines is how to align the necessity to control healthcare expenditures with creating sufficient incentives for innovations addressing public health needs. In most European countries, a variety of pricing and reimbursement policies have been implemented during the 1990s and 2000s, primarily in response to increasing pharmaceutical expenditures. Such policies included external price referencing, internal reference pricing, and the use of HTA and economic evaluation in reimbursement decisions. Yet, concerns over both the sustainability of healthcare costs, rewarding innovation, and cost containment continue to exist, prompting the question whether current policies are successful in achieving their intended goals.

The coming years therefore require a systematic and careful assessment and evaluation of the different tools and policies available, a refinement of methodologies, and an assessment of the impact on medicine use and pharmaceutical innovation. This will require significant investments and the involvement of stakeholders will be paramount in this process. Furthermore, it may result in the discovery of 'uncomfortable truths' and strongly diverging

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points of view of stakeholders will need to be accommodated. Simultaneously, the development and implementation of policies that will make for a truly sustainable and innovative European pharmaceutical sector in the long run are immense - for governments, companies, payers and patients - and therefore, an assessment and evaluation of tools and policies available is evidently needed.

We identified three key interlinked strategies that are available to regulators to control costs and reward innovation of medicines: managing price, managing volume, and managing which products will be reimbursed. Historically, policies have mainly focused on managing prices and managing reimbursement. In recent years two developments can be identified; first, it is increasingly being recognized that policies only serving a single policy goal such as cost-containment might not result in favorable long-term effects on innovation, and second, policies that impact *all* these factors (prices, reimbursement, and volume) might be most efficient in aligning conflicting policy aims. In line with these developments, HTA and value-based pricing have been identified as promising policies, but even though much research has been done in the field of economic evaluations, HTA, and pricing and reimbursement of medicines, a number of knowledge gaps remain. Further research is needed for the analysis of existing practices, for developing practical "tool boxes" and models for new approaches, and for studies that evaluate the introduction of new policies. In addition, this knowledge and (country-specific) experience should be appropriately communicated and disseminated, e.g. via networks for policy-makers.

European countries currently use a range of policy options that aim to control pharmaceutical expenditure, stimulate innovation, and ensure financial access to medicines. External price referencing is the predominant pricing policy in Europe and is increasingly being used outside of Europe as well. Payers are motivated to use external price referencing as a tool to contain prices of new on-patent medicines. Evidence for both intended effects (lower prices), as well as externalities of the policy, is mixed and sometimes contradictory. The impact of external price referencing on price levels throughout Member States, the distortion of the system due to confidential discounts and rebates, the availability of medicines in lower income countries, delays in market launch, and potential long-term effects on incentives to innovate should be studied.

Even though it is unlikely that external price referencing will be replaced completely by other pricing policies in the short-term, the feasibility of implementing alternative pricing strategies and their impacts on incentives for innovation should be studied. Value-based pricing, which is currently used by Sweden and will be implemented in the United Kingdom in 2014, has been argued to enable efficient pricing together with providing long-term incentives for innovation. Evidence at this point, however, remains scarce and mainly theoretical. Evaluation studies of countries that have implemented or are planning to implement value-based pricing therefore are warranted.

There is widespread evidence that list prices throughout Europe do not reflect actual prices and therefore erode the cost-saving potential of external price referencing. External price referencing therefore could benefit from increased transparency of medicines prices particularly tender price information which are not affected by discounts and rebates and the support of initiatives for exchanging price information. Simultaneously, this could be seen as an important reason to consider alternative pricing strategies since the policy does not seem to achieve its intended goals - and other pricing and reimbursement policies, including



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value-based pricing, might have the potential to send clear signals to industry on what innovations are expected and valued by payers. Furthermore, this would enable payers to set prices that reflect their own willingness to pay for innovation, instead of having to rely on prices set by other countries and the success of other countries to achieve fair prices.

Many European countries are moving towards the use of HTA and economic evaluations in the reimbursement of medicines. Payers that consistently apply decision-rules in reimbursement based on cost-effectiveness, as well as other determinants, in the assessment and appraisal of medicines could provide an important positive incentive for pharmaceutical innovation. Existing initiatives of cooperation and networks within Europe and beyond improve evidence-based and informed national pricing and reimbursement procedures. Therefore, a continuation and expansion of cooperation and exchange of experience is needed. Research networks include EUnetHTA, CAPR and PPRI with international organizations such as Health Alliance International (HAI), the WHO and the World Bank (especially for networks between the EU and low- and middle-income countries). Existing networks such as EUnetHTA and the PPRI network could also provide a basis for future networks (e.g. by adding a more explicit academic component), and make important contributions to the development of methodology, such as generalizability and transferability of economic evaluations.

Many stakeholders expect an increasing role of EUnetHTA in joint reimbursement assessment, although joint assessment solely considers relative effectiveness of pharmaceuticals. Improvements in the methodology of cost assessment - especially considering the issue of transferability of economic evaluations - are needed. Such improvements could contribute especially to the quality of the data that small countries frequently need to rely on.

Pharmacotherapy at the interface of the outpatient and hospital sectors can be improved. At the moment these sectors operate as separate worlds from a pricing and reimbursement perspective in many countries. Legal and organisational aspects need to be addressed in order to abolish the duality in the system and to remove existing incentives to stakeholders for transferring treatments and patients between the in- and outpatient sector as stakeholders should be incentivized to define the best point of care, including pharmacotherapy, from a *therapeutic* perspective. Research is needed to explore the possibility of the implementation of policies applicable to both sectors such as joint reimbursement lists and joint therapeutics committees. The introduction of policies to improve interface management should be accompanied by evaluations. Interface issues are of at least equal importance in low- and middle-income countries.

Differential pricing and separation of markets must be possible in Europe to reflect differences in ability to pay for medicines between countries, especially in light of the economic crisis that has severely affected a number of European countries. Policy options that would facilitate differential pricing need to be studied and developed. The development of differential pricing models is currently very challenging due to the complex EU policy environment and the interaction of parallel trade and external price referencing. The extent of the impact of external price referencing and parallel trade, in terms of availability of medicines and the affordability of medicines in EU countries, and the impact of such policy for all stakeholders, should therefore be evaluated.



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There is increased recognition for the fact that price is only one determinant of pharmaceutical expenditure and that effective policies should consider volume as well. It can be expected that in the coming years, new and more adaptive policies will be developed for high cost and high volume medicines, with an increasing role for managed-entry agreements and HTA for such medicines. Furthermore, effective generics promotion policies need to be investigated before effective interventions can be implemented, as many countries still could achieve substantial savings through high uptake of generics combined with policies that result in low generic prices, including tendering.

In addition, more adaptive approaches to pricing and reimbursement need to be developed in order to account for the increasing role of HTA and economic evaluations, as well as the expected increase of rare disease medicines and stratified medicines (see Background Paper 6.19 and 7.5). Whereas many countries now determine a medicine's price at a single point in time (usually at market entry), moving towards adaptive pricing would allow for managed-entry agreements, price-volume agreements, as well as the re-evaluation of prices when new indications are added for a marketed medicine. Particular attention might be required for high-cost medicines and new approaches such as joint procurement of countries and new integrative funding models might be warranted. In particular, research is needed regarding orphan medicines and their high costs, due to the low number of data generally available for informed decision-making. Furthermore, societal support for high prices, equity considerations, and potential cooperative structures in data collection for cost-effectiveness evidence should be investigated.

Pricing and reimbursement policies play a crucial role in stimulating the future development of medicines addressing unmet medical needs through creating appropriate incentives for innovation. Within Europe, pricing and reimbursement decision-making takes place at the national level and there is much variety in policies and practices. Notwithstanding, dialogue and cooperation between countries, institutions, and stakeholders is needed at both the political as well as the technical level in order to facilitate long-term positive impacts on innovation. Formalised cooperation structures between regulators involved in marketing authorization and competent authorization for pharmaceutical pricing and reimbursement could further aid the improvement of the current European policy landscape for pricing and reimbursement.

## Cost-containment policies in public pharmaceutical spending in the EU

Carone G, Christoph Schwierz C, Xavier A. 2012

Report of European Commission providing about pharmaceutical policies applied in EU Member States

### 19. Summary and conclusions

This paper presents a description and an evaluation of policies aimed at containing public spending on pharmaceuticals in the EU.

Pinning down policies which favour the rational use of medicines and strengthen the sustainability of public finances is not an easy task, as in-depth assessment of the cost-effectiveness of different measures is still scarce, though growing. However, on the basis of past experience and cases studies, the following broad guidance can be drawn:

- **The decision to pay for a medicine with public money should be transparent, based on relevant criteria and the decisions should be revisable** (Le Polain et al. 2011). This is important, because decisions often have to strike a balance between conflicting objectives of health systems, such as sustainability of public finances, equity and quality of care. Health-technology assessment (HTA) contributes to evidence-based decisions and identifies those medicines which offer the highest value for money. Whilst HTA is mostly used to evaluate medicines, medical devices, clinical procedures and public health interventions are increasingly subject to HTA. Whilst many countries already define explicit objective assessment criteria in line with



HTA criteria and procedures, in practice, the decision-making process is often not transparent and could be substantially improved.

- **Reimbursement decisions for pharmaceuticals should be revisable**, as there is risk that, over time, with development of new pharmaceuticals and based on additional empirical evidence, cost-ineffective medicines remain reimbursable, generating expenditures with no or little value added for the treated patients.
- **External reference pricing (ERP) gives the authorities a tool to control prices and thus to set one key parameter of expenditures (besides volume)**. It is also a relatively transparent pricing method and may lead to rapid savings by referencing to low-price countries. Price control should, nevertheless, be supplemented by other policies, including demand-side policies promoting the rational use of medicines.
- **Rebates, clawback and payback policies are widely used and powerful policy tool for cost-containment**. In case of payback, they also significantly increase the predictability in public pharmaceutical spending. These policies should nevertheless be aligned with existing or additional incentives for rational use of medicines aimed at the distributors of medicines and physicians, as these are also decisive for controlling the volume of pharmaceuticals sold.
- **Internal reference pricing (IRP) is a useful cost-containment policy**. When implemented so that it reinforces price competition and favours generic penetration, it generates savings without any reported adverse health effects or negative impact on innovation. As such, it may be preferred to free pricing schemes, even if it foregoes all potential savings that may be reaped in free pricing markets. IRP should be backed up by other policies increasing generic penetration, as these will increase the market share of generics and thus allow for reducing the reference prices further.
- **Allowing pharmacies to operate generic substitution leads to lower expenditures**. It also leads to reduced product prices and an increase in the use of cheapest interchangeable medicines. As such, further extension of generic substitution to cover more European countries bears a high potential to generate budgetary savings.
- **In order to enhance the use of generics, granting marketing authorisation and pricing and reimbursement decisions should be accelerated**. Firstly, pricing and reimbursement could be combined in the same process and delinked from patents, thus allowing taking these decisions already before a patent expires. Directive 2001/83/EC already provides a framework for speeding up the registration and marketing authorisation of generic products. The establishment of a Community patent and a unified specialised patent litigation system in Europe could avoid extensive delays to market entry of generics and generate savings for the public payers.



However, as on-patent pharmaceuticals appear to be the key drivers of increases in expenditures, generic substitution and other policies aimed at enhancing the share of generics can only partially contribute to cost-containment. Improving the value for money of patented pharmaceuticals, including through HTA remain an important policy priority.

- **Tendering is a well-established and successful tool for purchasing pharmaceuticals in the hospital setting but also more and more so in outpatient setting.** It has a substantial cost-containment potential, through considerable reductions of prices. Several EU Member States could make a more systematic and extensive use of tendering procedures. A possibility to be explored in future is international tendering by a group of countries.
- **Cost-sharing may improve the rational use of medicines as patients are made more cost-aware and therefore demand cheaper generic pharmaceuticals.** However, it is important that it does not lead to a decreased use of essential pharmaceuticals, thus negatively impacting on health. Cost-sharing has to be well designed to ensure the use of cost-effective medicines, while exempting the most vulnerable and avoid regressive financing of the system.
- **Tools for improving prescribing behaviour of doctors are widely used in the EU and may be regarded as standard policies aiming at the rational use of medicines.** Combining different policies, such as electronic prescription, monitoring and guidelines linked with electronic systems and providing feedback to physicians appears an effective way of improving prescription behaviour. In addition, education and information tools should be enhanced where possible. INN (active substance) prescription and prescription quotas, possibly coupled with target budgets and financial incentives have been shown to be effective tools for cost-containment purposes. This may reduce the risk of over-prescription and wrong co-medication.
- **EU institutions could help addressing the lack in transparency of pharmaceutical prices across European countries,** which contribute to the fragmentation of the internal market.

To conclude, it is worth stressing that a successful cost-containment policy in public pharmaceutical spending requires a comprehensive regulatory framework of pharmaceutical markets, with a broad set of measures, in order to be able to address "strategic" behaviour and create appropriate incentives for all stakeholders.



# Differences in costs of and access to pharmaceutical products in the EU

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Kanavos P, Vitoras S, Irwin R, Nicod E, Casson M. 2011  
Report for the European Parliament

Policy Department A: Economic and Scientific Policy

## EXECUTIVE SUMMARY

This report has been prepared at the request of the Committee on Environment, Public Health and Food Safety (ENVI) of the European Parliament. It aims to contribute to a better understanding of why pharmaceutical prices and public pharmaceutical expenditures vary across Member States.

While Member States have the primary role in providing health care for EU citizens, the 2009 Lisbon Treaty has given the European Union a greater role in the area of public health, including in the exchange of best practice regarding Member State activities.

Pharmaceutical prices are a key issue for health care, as medicines represent the third most important cost component in Member States' health care budgets. These costs are substantial and are rising faster than Member States' GDP, mainly due to an ageing population and the increasing cost of developing new pharmaceutical technologies.

At the same time, the regulation of pharmaceutical prices will affect an industrial sector that is a major component of Europe's economy in terms of employment, manufacturing, and research and development (R&D).

This report reviews the differences among Member States in terms of several key areas:

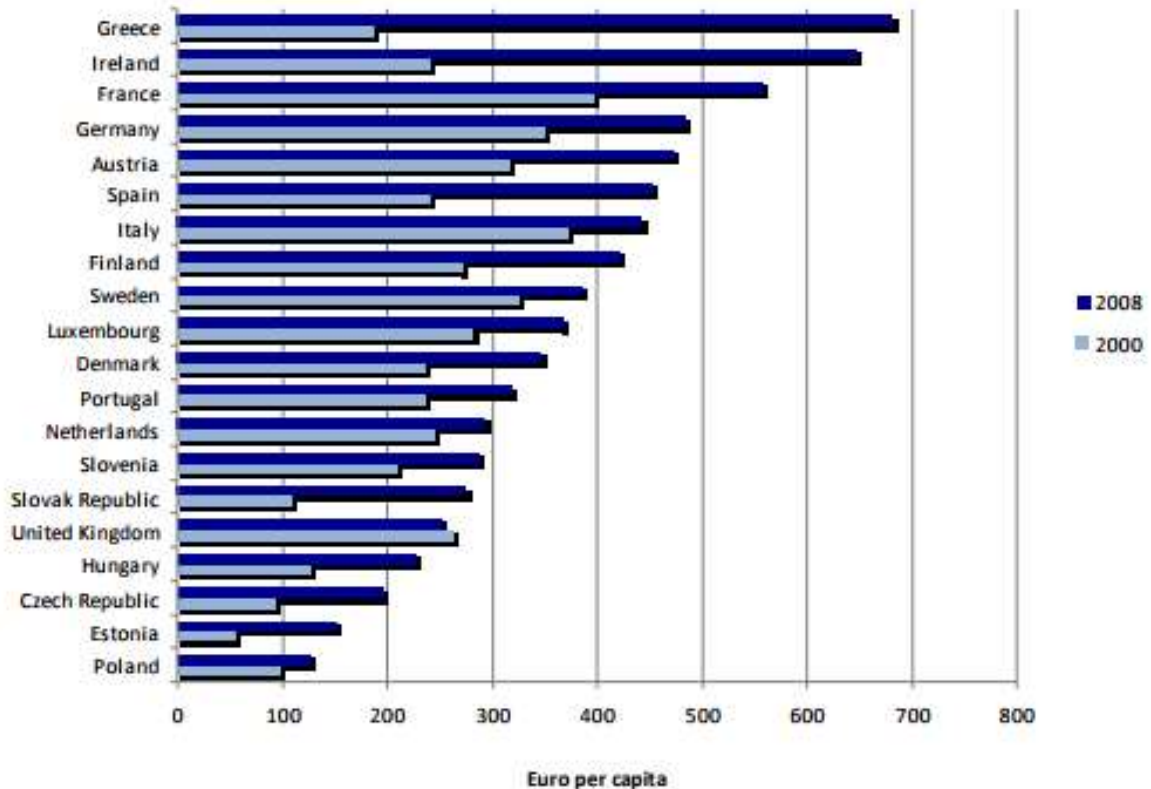
- Expenditure on pharmaceuticals that are reimbursed by health systems
- Prices of pharmaceuticals
- Pharmaceutical production and research

The report then studies possible reasons for the differences in pharmaceutical prices. It discusses the complexity of interactions among different regulatory measures used by Member States and their impact on pricing, cost-containment, innovation and access to pharmaceuticals.

### Differences in pharmaceutical prices and expenditures across Member States

Member State spending per capita on pharmaceuticals varies significantly (see Figure 1 below). This appears to be due to a range of factors: the amount of pharmaceuticals that are consumed; the mix of pharmaceutical products (brands versus generics); and their prices; as well as the share of the price that is reimbursed by national health systems.

**Figure 1: Total Pharmaceutical expenditure per capita (Euros), 2008 compared to 2000**



**Source:** OECD Health Data 2010 - Version: June 2010

Note: 2009 data for Greece (from local health insurance sources); 2006 data for Portugal; instead of 2000 data for the Netherlands and Poland, 2002 data are used. The reduction in the UK is attributable to the sterling depreciation against the Euro.

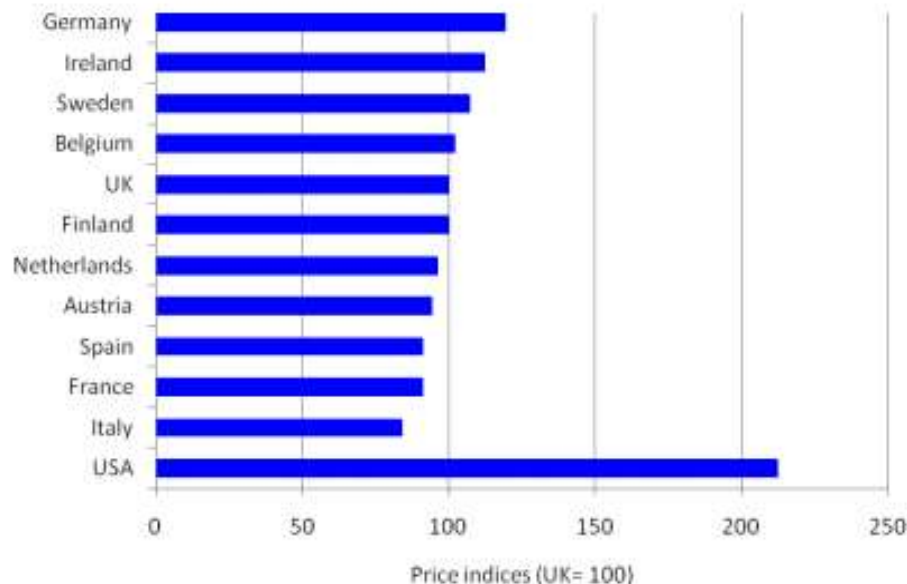
The prices of the pharmaceuticals themselves also vary across Member States. A recent review of the prices for 150 pharmaceuticals shows that the average price for this "basket" among 11 Member States found a 25% difference between the lowest and highest Member States (UK Department of Health, 2009), as shown in Figure 2, below. (Prices in the USA are significantly higher than any of the 11 Member States.)

Price variation for an individual pharmaceutical product can be even greater. A key distinction is between pharmaceuticals that are covered by patents and related forms of intellectual property rights (including market exclusivity periods and supplementary protection certificates) and pharmaceuticals that are not: in the former, the manufacturers hold a monopoly. For pharmaceuticals covered by patents, variations in price among Member States of up to four to one for a single product have been observed (Kanavos and Costa-Font, 2005).

For price variation assessment purposes, "orphan" medicines, i.e. those for rare diseases, can be assimilated to patent-protected medicines.



**Figure 2: Price comparisons among EU Member States (and with the US) for a basket of 150 pharmaceutical products; 2008 price index with UK=100**



UK Department of Health, 2009

For pharmaceuticals no longer covered by patents, "generic" versions can compete with those produced by the original manufacturer. Generic versions can cost much less, typically one-quarter of the price of the original, "branded" pharmaceutical. In this market, the variation in price can be even greater: the difference between the highest and lowest prices for one generic medicine for hypertension was found to be 16-fold (Kanavos and Casson, 2011 forthcoming). This is important, as a large share of the medicines consumed across the EU-27 is no longer covered by patents. However, the share of generic pharmaceuticals purchased also varies across Member States: it is over 50% of the total volume of pharmaceuticals consumed in the UK, Germany, Denmark and Sweden, but lower in most other Member States.

### Pharmaceutical production and research

The level of pharmaceutical prices (and the methods for price regulation) will affect the pharmaceutical sector, which directly employs 633,100 people across Europe and spends in excess of €26 billion annually on research and development (R&D). Production takes place in several Member States, but the bulk of manufacturing is accounted for by only a few: France, Germany, Ireland, Italy, Spain and the UK. The location of manufacturing can be explained in part by the size of domestic markets; another important factor has been the business environment.

Research and development is a critical component of the pharmaceutical sector, and the EU is the world leader in terms of pharmaceutical R&D spending, slightly ahead of the United States.

Basic and discovery research is concentrated in several Member States: on a per capita basis, Denmark and Belgium are leaders, followed by Sweden, the UK, France and Germany. Developmental R&D (including clinical trials) is carried out across the EU. Member State policies regarding the pricing and reimbursement of new pharmaceuticals clearly have an impact on the industry and its incentives for devoting resources to innovation.

### **Key factors influencing the differences in pharmaceutical prices**

The important price differences across Member States can be explained by a number of factors.

One broad factor is national income per capita: in general, prices of in-patent pharmaceuticals seem to be proportionally higher in Member States with higher levels of per-capita income. In addition, higher-income Member States appear to spend more on pharmaceuticals.

A second key factor relates to Member State national (and, sometimes, regional) regulatory approaches. Member States use a variety of tools, both on the supply side (for determining both prices as well as the share of prices that are reimbursed) and on the demand side. The latter can include policies to encourage physicians to prescribe and pharmacists to dispense lower-priced generic pharmaceuticals, as well as requirements that patients pay a share of pharmaceutical costs.

On the supply side, Member State health systems usually negotiate prices with manufacturers based on a range of methods and criteria, and this is a factor in the price differences for pharmaceuticals, both those covered by patent and those for which the patents have expired.

A widely used tool (by 24 out of the 27 EU Member States) for determining prices is external price referencing. Under this mechanism, a Member State sets a pharmaceutical's price based on a comparison with prices in other Member States. This approach can lead to lower pharmaceutical prices, in particular when a Member State makes decisions based on the lowest comparison prices rather than an average. There are concerns, however, that it ignores other aspects, such as health priorities for each country, and moreover that it can create uncertainty for innovative sectors of the industry.

Tendering for off-patent pharmaceuticals in primary care (i.e. outpatient care) has been used in a few Member States, including the Netherlands and Germany, where it has led to a significant reduction in prices. Some Member States have also used price caps for generic pharmaceuticals, but a review suggests that price levels are lower in Member States that do not use this approach (Puig-Junoy 2010). Internal reference pricing is also used extensively to promote generic use and, through that, achieve savings for health systems.

Reimbursement decisions also affect price. Member States can establish a formulary that lists pharmaceuticals that are reimbursed by health care insurance (or a negative formulary, for those that are not reimbursed). A key method for reimbursement decisions in the context of in-patent pharmaceuticals is Health Technology Assessment (HTA): it is increasingly used to appraise the additional clinical benefit of new pharmaceuticals against existing ones, in relationship to their respective costs.



Its results are used primarily to make reimbursement decisions. However, as Member States have different ways of accepting evidence and interpreting it, variations exist in the application of HTA appraisals and these can result in different prices as well as diverging coverage decisions for the same pharmaceutical across different Member States.

The level of value added tax (VAT) will also affect prices: the rate for pharmaceuticals varies across Member States from zero (e.g. UK and Sweden) to 25% in Denmark. Some Member States such as Greece have recently raised VAT rates for pharmaceuticals.

Another factor influencing pharmaceutical prices is the margin taken by wholesalers and retailers: this too differs greatly across Member States. Government policies can influence these margins, can set requirements for the number of pharmacies and can encourage or limit the consolidation of companies in the wholesale and retail markets. In those Member States where allowed, some manufacturers have put in place direct sales to pharmacies, or chosen to work with a restricted number of wholesalers, methods that can indirectly reduce the overall cost of distribution.

The EU single market allows distributors and other market actors to purchase pharmaceuticals in Member States with lower prices and re-sell them where prices are higher. The market share of parallel-traded pharmaceutical products in the main importing Member States stands between 1.7% in Finland and 16.5% in Denmark (EFPIA, 2010). This practice, which has been reviewed and upheld by the European Court of Justice, has been cited as a mechanism that can reduce prices in the sales markets. Overall, however, it appears that the final sale prices of pharmaceuticals have not been significantly reduced by parallel trade. In other words, most of the difference in price accrues to the intermediaries (Kanavos and Costa Font, 2005; Kanavos and Vadoros, 2010). Manufacturers have turned to direct sales methods as a response to parallel trade.

### **Access to medicines**

The different Member State approaches regarding pharmaceutical prices and reimbursement have consequences also for patient access to medicines in terms of both availability and affordability. HTA appraisals for new pharmaceuticals covered by patent may be different in one Member State from those in another. As a result, the access that patients have to such medicines varies across the EU. In particular, access to certain categories of in-patent pharmaceuticals tends to be negatively correlated with market size and per capita GDP.

In some cases a low price for a new product in one national market can lead manufacturers to refrain from launching the product in other markets, since the low price might jeopardise their pricing prospects elsewhere due to the wide application of external price referencing.

A different problem is seen regarding generic medicines: here, manufacturers of generics may decide not to enter smaller markets. As a result, health systems and patients in these markets may not have access to these lower priced alternatives. Small markets face similar problems for new orphan medicines.

Parallel trade has also raised concerns regarding access to pharmaceuticals, as it has been associated with shortages in exporting Member States (Kanavos and Costa-Font, 2005, Gainsbury, 2009; Taylor, 2010).

### **Policy options**

The Lisbon Treaty has established a more important albeit limited role for the EU in health care policy. The EU can organise and further the exchange of best practice and carry out monitoring and evaluation of Member State health care systems.

One option could be to strengthen the sharing of information and policy experience among Member States on mechanisms used to purchase pharmaceutical products. This could be done by building on existing initiatives such as the network of Competent Authorities on Pricing and Reimbursement. An exchange of information could be used to identify good practices at the Member State level. Approaches to Health Technology Assessment (HTA) could be a key topic of further discussion, given that a growing number of Member States use this approach, but their results in terms of reimbursement decisions often vary. Clinical cost-effectiveness is one of the factors considered in HTA analysis. Here, EU institutions could foster stakeholder discussions to help define the value of innovation for patients, health systems and the EU pharmaceutical industry and its role in the European economy.

Deeper coordination among Member States in the field of biomedical innovation could avoid duplication in research efforts by national competent bodies. Setting research priorities in accordance with unmet medical needs at EU level would likewise be desirable.

EU policies can also encourage greater and earlier use of generic medicines, which could lead to significant price reductions in a number of markets.

Parallel trade also deserves further study and exchange of information at EU level.

Other options for attention include the problem of small markets, which face lower competition from generic pharmaceuticals and thus higher prices, as well as the problems related to the lack of availability of certain products in individual Member States. The EU could seek to identify mechanisms to address these issues.



# Pharmaceutical Pricing Policies in a Global Market

OECD, 2008

OECD report about pricing policies in several countries

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## Executive Summary

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*Variation in per capita expenditure on pharmaceuticals is relatively low across OECD countries...*

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The average OECD country spent 401 USD [measured in purchasing power parities (PPPs)] per person on pharmaceuticals in 2005, and half of OECD countries had per capita spending within 20% of the average. The United States had the highest level of per capita expenditure, at 792 USD PPP, and Mexico the lowest, at 144 USD PPP, just 18% of the US amount.

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*Variation in the volume of pharmaceutical consumption and in pharmaceutical retail prices are similarly low*

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France and Spain had the greatest volume of pharmaceutical consumption (an estimate derived by adjusting pharmaceutical expenditures for cross-country differences in the average retail pharmaceutical price level) per person in 2005, followed by the United States and Australia. All of these countries had below-average retail pharmaceutical price levels in 2005, with the exception of the United States, which had retail prices about 30% above the OECD average. Canada and Germany had price levels similar to that of the United States, exceeded by Iceland (159%) and Switzerland (185%).

Mexico had the lowest volume of pharmaceutical consumption per capita - less than a quarter of the OECD average and less than half that of Poland, the second-lowest country - but was not among the countries with the lowest average retail pharmaceutical prices. The lowest-priced countries were Poland, Turkey, the Slovak Republic, the Czech Republic, Korea, Greece, Hungary, Spain and Australia, all of which had retail pharmaceutical price levels between 68% and 81% of the OECD average.

Cross-country differences in retail prices reflect factors other than differences in the prices manufacturers charge. They also include distribution costs and - in many countries - value-added tax, which together can account from only a small share to more than one-half of the price paid by the end purchaser.

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*A country's income per head affects its pharmaceutical consumption, retail prices and expenditure levels, but other factors are at work*

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In general, income per capita is positively correlated across countries with the volume of pharmaceutical consumption and expenditure per capita. However, income is not the whole story. In fact, per capita income explains only one quarter of the variability observed in per capita volumes of consumption across OECD countries, and even less of the variability in expenditure and retail price levels. This is consistent with findings from research indicating that pharmaceutical demand varies across countries and is relatively income-inelastic – meaning that expenditure changes with income, but not as fast as income does.

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*Despite rapid growth, spending on pharmaceuticals accounts for a minor share of health expenditure in most OECD countries, though there are a few exceptions*

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Growth in pharmaceutical expenditures greatly exceeded the rate of growth in other types of health expenditures throughout the 1990s. Although pharmaceutical growth has since slowed while other health expenditures have increased more rapidly in recent years, growth in pharmaceutical expenditures continues to exceed the average growth of OECD economies. Nevertheless, the pharmaceutical sector accounts for a minor (average 17%) share of total health expenditure in most OECD countries. However, pharmaceutical expenditure accounted for about one third of health expenditure and more than 2% of GDP (compared with an OECD average of 1.5%) in Hungary and the Slovak Republic.

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*Out-of-pocket payments are relatively important sources of financing for pharmaceuticals*

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Private sources play a bigger role in financing of pharmaceutical expenditures – accounting for 40%, on average – than of other components of health spending, although the bulk of pharmaceutical spending is publicly financed in all but four OECD countries (the United States, Canada, Poland and Mexico). Out-of-pocket spending is generally more significant than private health insurance, which is an important source of financing for drug spending in only a handful of countries (the United States, Canada, the Netherlands and France).

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*The pharmaceutical industry plays an important role in the economies of several OECD countries*

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All of the top-15 firms in terms of global pharmaceutical sales have their headquarters in OECD countries, with about half in the United States and half in Europe (France, Germany, Switzerland and the United Kingdom). Production and R&D activities are undertaken in many countries, not only (or even primarily) in the country where the firm has its headquarters. The United States accounts for 39% of global pharmaceutical production, slightly more than the 36% European share. Pharmaceutical production accounts for a notable share of national income in Ireland (11% of GDP) and Switzerland (3% of GDP), the



two biggest net exporters of pharmaceuticals. Pharmaceutical industry R&D activities are relatively more important to the economies of Sweden and Switzerland, accounting for about 0.5% of GDP in those countries.

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*Parallel and cross-border trade accounts for only a small fraction of the value of the market*

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The practice of importing pharmaceutical products from a lower-priced country to a higher-priced one, either for sale (so-called “parallel trade”) or for personal use (so-called “cross-border trade”), receives considerable policy attention. Parallel trade is most significant between EU countries, but even so only accounts for an estimated 2% of the EU market. Canadian cross-border trade with the United States peaked in 2004 at about 8% of total Canadian sales, which represented only 0.5% of the US market in terms of value.

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*The products of ten large firms account for much of the global pharmaceutical market*

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In 2006, the top ten pharmaceutical firms accounted for nearly half the value of global sales. The market for pharmaceutical products is increasingly a global one, with trade and policy practices making market segmentation and corresponding price differentiation by country difficult – particularly within Europe, where multinationals have encouraged their subsidiaries to set prices within narrow price corridors. New active ingredients are launched in an average of ten countries, although manufacturers often release multiple versions of their on-patent products in different markets to reflect consumer preferences and to reduce opportunities both for prospective buyers to make external price comparisons and for wholesalers to engage in parallel trade.

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*The United States is the predominant market in terms of pharmaceutical sales value*

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Nine OECD countries account for about 80% of the value of global sales of pharmaceuticals. The United States, with a 45% global share, is the world’s largest market, followed by Japan, which accounts for 9% of global sales, France (6%), Germany (5%), the United Kingdom (4%) and Italy (4%).

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*Most sales revenues derive from on-patent products, rather than generics, with value concentrated in a relatively small number of therapeutic classes and successful products*

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Just ten therapeutic classes of drugs accounted for 36% of total global sales in 2006, a year in which approximately 105 original products were considered “blockbusters,” i.e. each generating more than 1 billion USD in annual sales. By contrast, generic products accounted for just 14% of the global market in terms of value, although more than 40% of products sold in several large markets, including the United States, Germany and the United Kingdom, are generics. Generics have less than a 10% share of the market in terms of both volume and value in Italy, Belgium, Spain and Portugal.

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*The prices manufacturers receive for their products vary across countries, although there is less variation in prices for the most innovative products*

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Japan, Switzerland and the United States have been identified in the research literature as countries with particularly high ex-manufacturer prices for patented medicines. Japan and Switzerland also have high ex-manufacturer prices for generic products. Studies have found that ex-manufacturer prices vary according to national income per capita, although there were important exceptions. In particular, such prices were higher than expected in some low-income countries, including Mexico. Another study found that there is less cross-country variation in ex-manufacturer prices for those products representing significant innovation.

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*In spite of continuously increasing R&D investment, output of new drugs has declined and most pharmaceutical innovation has been incremental*

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Because most R&D initiatives are unsuccessful in bringing a new product to market, the total amount of investment per successful drug – an indication of the “productivity” of R&D spending in the pharmaceutical industry – is very large. A decline in productivity has been evident since the mid-1990s, as increased R&D investment has coincided with a decline in the number of new chemical entities approved for marketing.

As is true in other industries, most pharmaceutical innovation has been incremental, rather than radical. Most such innovation has little or no added therapeutic value over existing treatments.

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*The pharmaceutical industry uses a range of techniques to maximise profits over a product's life cycle*

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Since marginal production costs are relatively low, maximising profits translates into maximising cash flows during the life of a product. In each market where sales would be expected to enhance a product's global profitability, pharmaceutical firms endeavour to launch products quickly at the price that maximises prospective profits. Firms try to extend the period of market exclusivity and to engage in promotional activities that aim both to capture as large a market share as possible and to increase the potential market.

By some estimates, pharmaceutical marketing expenditures account for a share of firms' outlays that exceeds that of R&D expenditures. Furthermore, the costs of doing business in different countries vary, depending on factors such as the burden imposed by regulatory compliance, the types of marketing and/or advertising activities permitted and the exposure to liability for safety or quality problems.



*Prices are not the only factor determining profits*

Because marginal costs of producing most pharmaceuticals are very low relative to the cost of research, development and bringing a product to market, firms can make volume-price trade-offs that result in equivalent sales revenue and profits for the industry, provided spillover to other markets can be prevented. Pharmaceutical firms have therefore made with public and private purchasers and third-party payers confidential agreements that provide discounts and rebates linked to the level of product sales.

*Widespread health insurance coverage distorts the market for pharmaceuticals*

The coverage schemes that subsidise the amount individuals spend on pharmaceuticals and protect them against the risk of incurring high out-of-pocket costs also distort the pharmaceutical market, affecting both prices and volumes of consumption. They define the degree to which the pharmaceutical market is subsidised, with greater subsidies resulting in relatively lower consumer price elasticity of demand. While there is great cross-country variation in cost-sharing requirements, individuals in OECD countries typically bear much less than half the cost of their pharmaceutical consumption, resulting in consumption that is greater than it otherwise would be if individuals paid the full cost. Beyond this, coverage schemes differ importantly in the extent to which they seek to manage the volume and mix of pharmaceutical consumption, with many coverage schemes having few restrictions on choice by physicians and patients while others are active in efforts to affect physician, pharmacist and/or patient decision-making.

*The global market for original medicines is competitive*

Unlike sellers of most health services in OECD countries, research-based pharmaceutical firms operate globally and thus do not face a single purchaser wielding monopsony power. Firms can and do choose not to launch their products in countries where doing so is not profitable. On the other hand, the manufacturer of an on-patent medicine normally has a monopoly on sales of a particular product in a particular market, although the product may be subject to competition from therapeutic alternatives.

*Specific characteristics of the pharmaceutical market have given rise to pharmaceutical price regulation in most countries*

The perceived potential for manufacturers to exploit a monopoly position when facing relatively inelastic demand for medicines has led many countries to regulate prices for at least some portion of the pharmaceutical market. Two countries with pluralistic coverage schemes – Canada and Mexico – have established price regulation for on-patent pharmaceuticals intended to assure that prices paid by any part of the population, insured or not, are not excessive. In most other OECD countries, coverage schemes require manufacturers to accept price limits in exchange for subsidisation through reimbursement schemes, which



act as *de facto* regulation for that part of the market covered by reimbursement. Even in the United States, manufacturers must submit to price regulation if they wish to be reimbursed under Medicaid and the Veterans Health Administration, the public schemes providing coverage to 19% and 2.6% of the US population, respectively.

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*Market-based or "free" pricing is common for products not subsidised by coverage schemes*

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Except in Mexico and Canada, where the prices of all on-patent medicines are subject to regulation, over-the-counter (OTC) products are normally not subject to price regulation unless their purchase is reimbursed by a coverage scheme. In a minority of OECD countries, including Denmark, Germany, the United Kingdom and the United States, firms are not constrained in setting either OTC or prescription drug prices at market entry, irrespective of the product's reimbursement status.

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*Several types of practices are used to limit prices and define reimbursement amounts*

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Regulatory authorities use a common set of tools to limit the prices charged by pharmaceutical firms. The most commonly used methods involve comparing proposed prices for new products against those prices paid by other payers, a practice known as external price referencing, or against those prices already paid for products judged to be similar, a practice known as internal price referencing. Pharmaco-economic assessment is used by some schemes as a means of making a formal judgment as to value provided, in terms of benefits and costs. There are a limited number of other approaches used, including profit controls, which serve as an indirect form of price regulation. Pricing policies are not limited in focus to the payment received by pharmaceutical firms; regulation of the distribution chain is undertaken in many systems.

With the exception of profit controls, public and private payers and purchasers of pharmaceuticals use the very same approaches to define the acceptable payment or reimbursement price. In the context of reimbursement, so-called reference price systems are often used to set common reimbursement amounts for products judged to be equivalent or similar, leaving patients to pay any price difference out-of-pocket. In cases where generic substitutes or therapeutic alternatives are acceptable, purchasers in some markets obtain low prices using tendering processes that require sellers to bid for an agreed volume of sales.

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*Pharmaceutical prices are determined by the respective market powers of the parties involved*

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In the case of the pharmaceutical firm, market power is determined by the perceived value of the product and the extent of competition from alternative therapies on the market.

In the case of the buyer (or payer), market power is determined by the size of the market represented – as measured in terms of the number of persons and their willingness and ability to pay – provided that the payer has the ability to act in ways that influence the

volume of a product consumed. While most OECD countries have a universal scheme that maximises market power by representing all or nearly all of the country's consumers, a few countries, such as the United States, have pluralistic schemes. Several large publicly financed coverage schemes and private insurers in the United States have enrolments that exceed the populations of some OECD countries.

The extent to which prospective buyers or third-party payers have the power to walk away from a transaction varies. Either regulation or competition to provide comprehensive coverage can limit their ability to deny patients reimbursement for a product that is categorically eligible for coverage. In particular, the power to walk away from a transaction is limited when a drug is in a monopoly position in a therapeutic area and is used in the treatment of a life-threatening disease. In such cases, both public and private payers experience public pressure to cover the drug. Thus, the ability to obtain price concessions often rests instead with the ability to influence the volume of the product consumed, by limiting reimbursement to particular circumstances or identifying preferred products.

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*Price regulation does not necessarily result in lower prices*

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While private insurers universally face pressure to extract the best possible price which their relative market power will permit, regulators and public schemes seek to balance cost-containment objectives with others, such as public health improvement, as well as industry policy goals and considerations of support for future pharmaceutical innovation, which may mean that they fail to push their market power as far as they might to obtain the lowest possible price. For this reason, it is not necessarily the case that price regulation will always result in lower pharmaceutical prices than would be obtained in an environment characterised by competing private insurers.

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*Many other types of policies, other than those directly related to pricing, affect the pharmaceutical market*

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While pricing policies have been the focus of attention in terms of their impact on pharmaceutical markets, other types of policies are important in their prospective impact on the timely availability of products in the market, the adoption and diffusion of those products, and the level of consumption of the product over its life cycle. Chief among these policies are those that affect market authorisation and those that set standards for enforcement of intellectual property rights. In addition, coverage schemes routinely employ policies aimed at modifying patient demand (in particular, cost-sharing requirements), often employ policies aimed at influencing pharmacists' dispensing (such as policies to promote use of generic alternatives to off-patent original medicines), and occasionally employ policies aimed at altering physician prescribing (*e.g.*, prescribing budgets).



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*Policy makers hold common objectives, but may weight them differently when trade-offs are required*

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Policy makers intervene in pharmaceutical markets to promote public health by fostering prompt, affordable access to effective medical treatments. But subsidising individuals' pharmaceutical consumption often results in pressure to contain overall costs. And payers are increasingly concerned with being able to demonstrate that they attain good value for money in their pharmaceutical expenditures. Trade-offs across these goals are required when conflicts arise among them and with industrial policy goals, as may occur depending on the economic significance of the pharmaceutical industry in the country in question.

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*There are shortfalls in access to effective medicines, even in OECD countries*

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Although the availability of medicines on the market varies considerably across countries, the implications for accessibility are unclear, since countries often grant exceptional access to drugs that have not (yet) been launched in a market. Heavy subsidies for pharmaceuticals provided by public coverage and private insurance, reasonable cost-sharing arrangements, exemptions of vulnerable patients and caps on out-of-pocket spending serve to limit the likelihood of access being threatened on affordability grounds in most OECD countries. More serious risks come from gaps in coverage, given that a few countries still have populations without adequate coverage to ensure affordable access to prescription medicines. Furthermore, access can be limited by decisions not to subsidise expensive drugs that are judged not to be affordable or cost-effective at the offered price.

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*Policy makers seek to restrain the rate of growth in pharmaceutical expenditures, although the optimal expenditure level is undefined*

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The variation in pharmaceutical expenditures across countries raises questions about whether and which countries may be over- or under-spending, although there are no agreed international benchmarks for making such assessments. Policy makers in OECD countries attempt to control pharmaceutical expenditures using a range of tools, including control of prices and/or volumes (e.g., benefits management strategies directed at physicians or pharmacists). Some countries use policies to control the level of spending for particular products (e.g., product-specific rebates) or for pharmaceuticals generally (e.g., claw-backs, patient cost-sharing).

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*Payers are experimenting with sophisticated approaches to purchasing and payment arrangements*

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There may well be scope to move to cost-control mechanisms, such as price-volume agreements, that focus on achieving the desired level of expenditure on pharmaceuticals. In France, for example, specific agreements are signed for some products with high risk of overuse or misuse, under which the pharmaceutical company will pay rebates when the



agreed volume of consumption is exceeded or when drugs have been misused. Risk-sharing arrangements, under which the price may be retroactively adjusted as information about utilisation and outcomes under normal use become available, have the potential to reduce the need to make a trade-off between the objectives of ensuring prompt access and getting good value for money, when faced with incomplete information about the relative efficacy and cost-effectiveness of a new product.

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*Improvement in meeting public health objectives may well be possible without sacrificing cost control*

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Efforts to improve value for money in public spending on pharmaceuticals could help free up resources that could be better spent enhancing the availability, accessibility and appropriate use of effective medicines. Many, if not all, countries have some room for improvement in this respect. They could get better value for their money by maximising the use of generic alternatives to off-patent original products, fostering erosion of the prices of off-patent products through greater competition, ensuring efficient distribution systems for prescription and OTC products, and becoming more sophisticated in their reimbursement pricing strategies.

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*Reference pricing is a practice by which payers seek to get good value for money in pharmaceutical expenditure*

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Under normal market conditions, informed consumers compare products to determine if added benefits are worth added cost. This is difficult in the case of pharmaceuticals, not only because information on relative benefits may not always be fully available at the time of decision making, but also because patients rely heavily on physicians to act as their agents in choosing appropriate medicines. The practice of setting a common reimbursement amount for similar products, leaving patients to pay the difference out-of-pocket if they use more expensive alternatives – a practice that is somewhat misleadingly known as “reference pricing” – is attractive in the sense that, theoretically, only those products valued by patients and their physicians should receive a premium price. In practice, however, manufacturers often prefer to price at the reference point rather than risk losing market share in imperfectly operating markets.

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*Pharmaco-economic assessment can help to ensure good value for money in pharmaceutical expenditure*

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A tool for evaluating a product's benefits relative to its costs, pharmaco-economic assessment can help achieve good value for money when incorporated into pricing and reimbursement decisions. Since its introduction into pricing and reimbursement processes by Australia and Canada in the 1990s, pharmaco-economic assessment has been incorporated in the pricing and reimbursement practices of many OECD countries in ways ranging from asking manufacturers to provide information on relative cost-effectiveness in support of applications for reimbursement to conducting original assessments of the

benefits that would be derived from use of a product and expected costs to payers or society generally. Experience from these countries demonstrates that pharmaco-economic assessment can be technically and politically feasible when employed in different types of health systems. It remains, however, a technically challenging and value-laden exercise, particularly when judgments about the value of a product for which there is no therapeutic alternative must be made.

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*Pharmaceutical pricing policies have an impact outside national borders*

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External price referencing (or international benchmarking) stands to affect the prices and availability of medicines outside the country undertaking the benchmarking practice by reducing manufacturers' willingness to set prices according to national market conditions. This may have a negative effect on affordability and availability of medicines in smaller markets and lower-income countries, including lower-income countries in the OECD. The practice of agreeing to confidential rebates can also have an external effect, in that other countries using external benchmarking may reference artificially high prices, resulting in list-price inflation. Claw-backs have a similar impact in that they mean the price is effectively changed post-purchase (after the list price has already affected the global price through external benchmarking). The convergence in list prices of pharmaceuticals that has been observed in Europe (including Switzerland) and between European countries and Canada is consistent with what would be expected in a market characterised by such practices.

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*Manufacturers have developed strategies to maximise profits in an increasingly global market*

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Even as globalisation has reduced opportunities to maximise profits through market segmentation and differential pricing, manufacturers have responded to the increasingly global market for their products in a strategic way. In response to external price referencing, they launch their products first in countries where they can set prices freely or can negotiate relatively high prices (often in the country where they have their headquarters), delay or refrain from launching in relatively lower-price countries and maintain artificially high list prices, even when they are willing to consent to confidential rebates. They use strategies to inhibit parallel trade, such as supply-chain management, litigation, lobbying and product proliferation (e.g., release of products with different formulations, strengths and package sizes). The latter technique also serves to limit opportunities for international price referencing. The success of these strategies is evident in that the pharmaceutical industry continues to be one of the more profitable industries in the global economy.

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*Profits reward past investment in pharmaceutical R&D and serve as an incentive for future investment*

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As in other industries, private R&D investment in the pharmaceutical industry is motivated primarily by expected returns on the investments, given scientific opportunities



(the state of the art in a therapeutic area or in a mode of production) and the comparative advantages of firms. The pharmaceutical products that make it to market are those that are viewed by the pharmaceutical industry as most likely to be profitable in terms of the conditions they target and the level of innovation they represent over existing alternatives.

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*R&D investment incentives are distorted by characteristics of the pharmaceutical market*

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Important characteristics of the pharmaceutical market call into question whether it is possible to obtain a socially optimum level and direction of R&D investment. In the case of prescription medicines, the combined impact of insulating patients from the cost of the medicines they consume and providing firms that produce innovative medicines with the exclusive rights to sell their products distorts market signals, creating a risk of over-investment in the development of new products. On the other hand, cost-containment pressures may lead regulators, payers and purchasers to make pricing and reimbursement decisions that establish profit signals for under-investment.

Beyond this, purchasing decisions made in the absence of full information may well distort the incentives firms face as to how to direct their R&D investments. Information on the effectiveness of new medicines, relative to therapeutic alternatives, is often not available to patients and the physicians who act as decision-making agents, and neither may have incentives to consider whether any added benefits are worth the cost differential.

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*Pharmaceutical pricing policies are among several policy variables that influence the expected returns on investment in R&D that in turn serve as an incentive to finance new investment*

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Methods used to establish relative price levels, particularly techniques by which products are differentiated for price premia, provide market signals that steer investment towards particular types of innovation. The most commonly used practice, external benchmarking, encourages firms to differentiate their products across countries so as to limit price comparisons. Such practices yield no therapeutic benefit and may come at the expense of other types of innovation. The practice of referencing prices or reimbursement amounts to therapeutic comparators, on the other hand, provides incentives for innovation that offers demonstrably more value than existing therapies and acts as a disincentive for incremental innovation that offers little or no improvement over existing therapies. However, therapeutic referencing only provides an indication of the new product's value if the price of the comparator product is reasonably reflective of its own value. This is not necessarily the case in the current pharmaceutical market environment, where third-party payers and regulators predominantly use external benchmarking of prices paid elsewhere to limit or define the prices of products that have no therapeutic comparators.



*Pharmaceutical pricing and reimbursement approaches using pharmaco-economic assessment establish incentives for investment in valued innovation*

In the interest of encouraging valuable innovation, efforts to link the level of expenditure for a given pharmaceutical product to the value of the benefits offered by the new product are attractive in that they can be used by manufacturers to assess willingness to pay for future innovations and should thus provide incentives for investment in R&D leading to valued innovation. Pharmaco-economic assessment can be used to reward and foster innovation with the greatest value to patients and society. To the extent that pharmaceutical producers profit more from innovations that have the greatest value to patients and society, they will face incentives to invest more in R&D to produce such therapies.

*Each country's policies will have only a marginal impact on future pharmaceutical innovation, except when there are spill-over effects*

Pharmaceutical R&D investment decisions reflect the industry's assessment of the future market with a global perspective. Therefore, the marginal impact of any one country's policies will be proportional to market size and thus minor (with the important exception of that of the United States). Nevertheless, features of national markets and national policy practices may encourage firms to invest in R&D in order to differentiate products and segment markets, especially when national policy impacts have spill-over effects on other countries' price levels. The practice of external price benchmarking means that early-launch countries in particular (and those that are most often selected by other countries for price references) are likely to have an impact on incentives for investment that is disproportionate to the size of the market. This suggests that it is particularly important that the prices established in those countries present an accurate reflection of the product's value, both in absolute terms and relative to other products on the market.

## Study on enhanced cross-country coordination in the area of pharmaceutical product pricing

Vogler S, Lepuschütz L, Schneider P, Stühlinger V. 2015

Report about external price referencing and differencing policies, mapping exercise and options for improvement / implementation

### Executive Summary

European patients and citizens need access to safe, effective and affordable medicines while the health care system should be financially sustainable, and innovation should be encouraged. This is perhaps the key challenge for the national competent authorities and public payers as pharmaceutical pricing and reimbursement remains the competence of EU Member States. In the light of increasing financial pressure while further new high-priced medicines are expected to come to the market, new approaches to achieve the above-mentioned objectives might be required. Without disregarding the subsidiarity principle, possible benefits of cooperative approaches should be studied and discussed.

In this context, a consortium of Gesundheit Österreich Forschungs- und Planungs GmbH, SOGETI Luxembourg S.A. and the University for Health Sciences, Medical Informatics and Technology was commissioned by the European Commission (DG SANTÉ / Chafea) to explore the pharmaceutical pricing policies of external price referencing (EPR) and differential pricing (DP) with regard to their ability to achieve two of the three above-mentioned policy objectives: to improve patients' access to medicines and to generate savings for public payers.

In particular, this 'study on enhanced cross-country coordination in the area of pharmaceutical product pricing' aimed to survey existing EPR schemes in European countries and to develop possible improvements to the current EPR practice, as well as to analyse how DP schemes could possibly be designed for European countries, including addressing identified constraints to DP in Europe. Furthermore, it should be explored how EU-level coordination mechanisms could support the improvement of EPR systems and the establishment of a DP scheme.

To achieve these research objectives, the authors relied upon a range of methods including a literature review, a survey of competent authorities for pharmaceutical pricing, interviews with procurement experts, price simulations, a legal analysis, research of cooperation models and SWOT (strengths, weaknesses, opportunities, and threats) analyses. Extensive reviews involving the services of the EC, stakeholders and academics ('peers') were performed to ensure the high quality of the report.

### External price referencing for medicines – Use and impact

External price referencing (EPR), also known under different names such as external reference pricing or international price comparison / benchmarking, is defined as the practice of using the price(s) of a medicine in one or several countries in order to derive a benchmark or reference price for the purposes of setting or negotiating the price of a medicine in a given country.

EPR is the most commonly applied pricing policy in European countries. As of 2015, apart from Germany, Sweden and the UK, all other EU Member States, as well as Iceland, Norway, Switzerland and Turkey, set the prices of (some of) their medicines based on price comparisons with other countries. In Germany, though the law provides for prices in other countries to be considered as an additional piece of information in pricing of new medicines, it is claimed that EPR is not applied in the follow-up procedure. In Denmark, EPR is only applied as a supportive pricing policy in the hospital sector. According to a survey undertaken in April/May 2015, 20 of the 29 countries that apply EPR use this policy as sole or main pricing policy. Typically, EPR is limited to specific medicines, such as originator, prescription-only or new medicines. The number of reference countries included in the basket varies between one country (Luxembourg) and 30 countries (Hungary and Poland). Countries most frequently referenced to are



France, Belgium, Denmark and Spain followed by Italy, the UK and by, to a lesser extent, Austria, Germany and Slovakia. Major criteria defining the composition of country baskets are geographic neighbourhood or a comparable economic situation in the reference countries.

The methodological specifications of how an EPR scheme is designed differ between the mentioned countries. For instance, 21 countries do the comparisons of medicine prices at the level of ex-factory prices, and eight countries at pharmacy purchasing price (wholesale price) level. The EPR applying countries refer to the officially published list prices, thus taking neither statutory nor negotiated discounts into account. Germany, though not applying EPR, specified in its law that discounted prices are to be reported by the manufacturers. The most commonly applied method to calculate a reference price is an average, or some kind of modified average, of the prices in the reference countries. The price data required for EPR are provided by the marketing authorisation holder in 23 countries, and 26 countries validate the price information provided. Though price monitoring is provided for in the legislation of 25 countries, it is actually done on a regular basis solely in 17 countries. These regular intervals vary between countries and range from three months to five years.

A literature review conducted as part of the study suggests that EPR has proven to be effective in generating, sometimes substantial, savings for public payers. The extent of savings has considerably depended on the methodology applied. There are lost opportunities due to discounts, rebates and similar arrangements in the reference countries that are not considered in EPR. As illustrated by simulations done by the authors of this study, it may be possible to achieve major impacts on price reductions by referencing to discounted prices and by performing regular EPR reviews. With regards to patient access, EPR is likely to have a negative impact since it incentivises the pharmaceutical industry to first launch in higher-priced countries and delay, and refrain from entering the market in lower-priced countries, and may also inhibit them from offering medicines at lower prices in lower-priced countries.

### **External price referencing – Options for improvement and cooperation mechanisms**

EPR is a pricing policy that considers the prices in other countries, but it is not a cooperation tool per se. However, both changes in the methodology undertaken unilaterally by countries as well as cooperative approaches between Member States can help improve the performance of EPR which is a resource- and time-consuming activity, and thus possibly positively impact the outlined policy objectives. The report discusses four options for improvement: 1) a central price database, 2) the consideration of discounts, 3) regular price monitoring, and 4) the coordination of EPR formulae.

A major tool to facilitate price comparisons could be a European medicine price database, such as the existing Euripid database of competent authorities of EU Member States and a few further European countries. According to its users, Euripid has proven to be extremely supportive for competent authorities when they carry out technical work related to EPR (price surveys, validation and comparisons). Thus, the authors consider a centralised price database as a promising cooperation mechanism that should be continued and possibly extended in future. It would be highly recommended to have a centralised database that covers all EU Member States. However, some countries may not be able to join a European price database (e.g. no possibility to share the price data of the own country due to a lack of ownership) which would limit the effectiveness of the database. A current limitation to a European price database is the provision of undiscounted list price data only. The inclusion of discounted prices could significantly improve the relevance and quality of such a database. If the inclusion of discounted



prices is not possible, it is recommended to consider alternative approaches, such as at least an indication in the price database of whether, or not, discounts have been granted to that product.

As the analysis has shown, EPR could provide lower prices if the price comparisons were done at the level of real prices paid by payers (discounted prices) instead of list prices. As a unilateral measure, EPR applying countries could take into account, as a minimum, statutory manufacturer discounts in the reference countries (e.g. Germany) that are officially published. However, this would only cover parts, possibly small ones, of the discounts granted. Higher savings might be generated if prices actually paid by public payers are referenced to, i.e. considering also confidential discounts, rebates, and similar financial arrangements in the other countries. One option to receive this information is a sharing of these data among Member States.

Another option to improve EPR would be regular price reviews with subsequent price revisions whose impact on reducing prices has been evidenced by simulations. However, industry could also benefit from regular price revisions if price increases (e.g. due to exchange rate fluctuations) were also considered. There is room for improvement since several Member States do not seem to perform regular (i.e. bi-annually, annually or at other defined time intervals) price re-evaluations even if provided for in the legislation.

Finally, another consideration could be the adaptation of the EPR formulae. For instance, countries could adjust prices by reference countries' purchasing power parities, rather than merely by nominal exchange rates, when performing EPR. This is a step that could be taken unilaterally by any EPR applying country. If several countries consider such changes, an exchange of information and best practice on criteria and methods for adjustment, which would support capacity building is recommended. A multi-national agreement on adjusting formulae in a particular method would be similar to the implementation of differential pricing in Europe (see below).

The four options presented can support policy-makers to improve the efficiency of performing price comparisons under EPR, and can help generating further savings for public payers. However, apart from the fourth option which contains traits of differential pricing, the other three options are not necessarily expected to impact the differentiation of prices between countries along the lines of ability-to-pay and thus improve access to medicines. The four options presented are not mutually exclusive, and it is recommended to consider a combination of these options.

### **Differential pricing for medicines – Use and impact**

Overall, differential pricing (DP) describes the strategy of having different prices for the same product charged to different customers. This study regards differential pricing which is understood as an international, governmental policy defining the prices of medicines according to the ability-to-pay, and/or the economic situation of the countries under DP. There is a difference to 'price discrimination' ('market discrimination', 'Ramsey pricing') that describes a business strategy of economic actors to segment the market according to the observed demand-elasticity of consumers and that is not the focus of this study.

Experience with DP exists with medicines for specific indications (particularly HIV/AIDS, tuberculosis, malaria, vaccines) that were procured under DP by international agencies and programmes (UNICEF, PAHO, GAVI, Global Fund, UNITAID) for low- and middle-income countries, including least-developed countries. There is no experience with DP, as defined above, applied for high-income countries, such as European countries.

The applied DP schemes aimed to ensure access to medicines that would otherwise have been unaffordable for these countries. Though the results are mixed, it was found that in some cases DP might have resulted in an improved access to medicines for low-income countries. In addition, there was some evidence that DP helped to reduce prices and thus made medicines more affordable. However, the entry of generic medicines into the market was seen to be more effective in driving prices down than DP.

It has been argued that DP may benefit manufacturers as well since they gain additional markets, and low profit margins in these markets might be out-weighted by increased unit sales.

Under specific conditions DP might serve as a, however second-best, policy option to ensure short-term access to medicines, particularly new on-patent medicines. It should be supported by other policy options including generic competition, joint procurement, voluntary licensing and compulsory licensing. A global legal framework for DP has been suggested by researchers advocating for access to medicines globally.

### **Differential pricing – Proposal for an EU coordination mechanism**

The report discusses a possible outline of a DP scheme for medicines in Europe as requested by the project tender specifications. This possible DP framework is described for analytical purposes, to illustrate what DP could mean in practice and to be able to assess its feasibility; but it should be noted that the authors do not necessarily recommend that a DP scheme should be implemented in Europe.

Such a scheme would require the agreement on principles and mechanisms of the countries included (in case of a collaborative approach for the EU, these were all 28 Member States) which is a challenge and might not be politically feasible in the short term. Mechanisms to be agreed upon would involve a maximum or minimum entry price, one of the biggest challenges by itself, and the size of the mark-ups or mark-downs. When designing such mechanisms, economic indicators, such as the gross domestic product or the purchasing power parities, should be taken into consideration. Some would argue that a DP scheme should be designed in a way that prevents higher prices in the higher-income countries compared to a situation without DP; others that these higher price levels might be justified.

In any case, if the DP approach is chosen, it is recommended to start with a pilot project for one, or a few products, defined according to some eligibility criteria (candidate medicines could include orphan medicinal products, or other high-priced medicines, for instance). EU Member States are advised to accompany any DP pilots, and later possibly regular DP schemes, by evaluations, with the possibility to feed-in lessons learned in future mechanisms. The pilots could be launched in cooperation with pharmaceutical companies interested in marketing their product in the European Union under a DP scheme. Trust and better planning between the two parties could be ensured if both supply and purchase guarantees would be integrated into contracts for medicines procured under DP. Notwithstanding the subsidiarity principle, operationally, the DP schemes would benefit from a central coordinating structure.

A key constraint that limits any differential pricing in Europe is parallel trade. Parallel trade occurs, if a genuine product originally sold under the patent protection is traded in another country without control or permission from the original patent holder. This leads to the re-importation of medicines from lower-priced to higher-priced countries and thus contradicts the principles of DP in which prices vary according to economic parameters. From a legal perspective, medicines as such are no exception to the free mobility of goods in the internal market. Thus, though parallel trade should not be

interfered with in order to not distort competition within the Union, export bans and notification/authorisation procedures related of exports of medicines might be justified if considered suitable, proportionate and necessary for achieving health and life protection goals. However, no legally binding Commission decision or European Court of Justice rule has yet been issued on this matter, although the effects of parallel trade on health and safe access to medicines remain a matter of strong controversy.

### **Policy options for the future**

The exact impacts of a possible DP scheme within the European market are still unclear. It is evident, however, that the implementation of a DP scheme would be extremely challenging and would require enormous political will to address legal constraints and achieve agreements between Member States on principles and mechanisms. However, the challenge of ensuring patient access to new, possibly innovative medicines has become an urgent need in the light of new high-priced medicines. Thus, while the implementation of a DP appears to be unfeasible in the EU in the short run, EU Member States could consider using DP traits in EPR schemes. In the short term, EU Member States could improve their EPR systems, particularly by doing regular price revisions and considering (statutory) discounts, but these measures primarily help generate savings, and do not necessarily improve access to medicines. Some of the latter measures can be taken unilaterally by EU Member States, and cooperation would mainly regard the exchange of good practise on the methodology to be employed.

Moreover, EU Member States could consider exploring other new pharmaceutical (pricing) policies such as joint procurement initiatives which were not within the scope of this study. It is recommended using fora, such as the stakeholder review meeting of this project, to openly discuss strategies among stakeholders on how to deal with new high-cost medicines.



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## **Review 1: External Reference Pricing Policy brief #1 Pharmaceutical Pricing Policies and Interventions**

WHO/HAI. 2011/2014

WHO/HAI review about external price referencing worldwide: a mapping exercise and evidence about impact

## EXTERNAL REFERENCE PRICING



### WHAT IS THE BASIS FOR THIS POLICY BRIEF?

WHO/HAI Review Series on Pharmaceutical Pricing Policies and Interventions. Working paper 1: *External reference pricing* by Jaime Espin, Joan Rovira and Antonio Olry de Labry, Andalusian School of Public Health. [www.haiweb.org/medicineprices/policy/index.html](http://www.haiweb.org/medicineprices/policy/index.html)

As part of the joint World Health Organization (WHO)/ Health Action International (HAI) Project on Medicine Prices and Availability, a series of in-depth reviews have been published on pharmaceutical policies and interventions that may improve medicine availability and affordability.

This policy brief summarises the key points from the review on external reference pricing (ERP), which included a systematic literature review and a survey of nine predominantly middle-income countries that use ERP.

*Page references to the review paper are given in parentheses.*

### SUMMARY CONCLUSIONS

#### What are the main advantages of external reference pricing (ERP)?

Compared to some other pricing policies, ERP requires less complex technical analysis and judgement.

#### What are the main disadvantages of ERP?

Meaningful price information can be difficult to obtain. Available price data may require adjustments based on limited information. A country using ERP is unable to set pricing criteria suitable for its own circumstances; it relies on pricing policies of reference countries which may use other criteria. Widespread use of ERP has prompted manufacturers to adopt international pricing strategies that may have negative effects on lower income countries through international price convergence at higher prices. Low-price reference countries may experience launch delays for new products. Manufacturers may reduce transpar-

ency of pricing practices in reference countries. ERP would become impossible if all countries applied it.

#### Is ERP appropriate for regulating all medicine prices?

ERP is most suitable for on-patent products, particularly those with new active ingredients. For off-patent products, lower prices may be achieved through other methods, including internal reference pricing and policies that encourage competition and use of low-priced generics. Health insurers and institutional purchasers have additional options to achieve more effective price control including a reference price system, competition for formulary listing and competitive public procurement.

#### Is ERP appropriate for all countries?

ERP has been used by a wide range of middle- and high-income countries.

Although the evidence of its effectiveness is limited, many countries have been satisfied with the use of ERP. Countries with high technical capacity or large pharmaceutical research bases may find health technology assessment more appropriate for pricing on-patent products. Evidence is lacking about the suitability of ERP for low-income countries.

#### Are there any complementary policies that should accompany ERP?

Price regulation is usually applied to patient prices. Policies are needed for adjusting the ERP derived from ex-factory prices to cover costs of importation, wholesaling/distribution and dispensing.

#### Are there any key pre-requisites for implementing ERP?

ERP requires capacity for enforcement and monitoring patient prices.



**What is the policy?**

ERP uses the prices of identical medicines in one or more reference countries to derive a benchmark or reference price for the purpose of setting or negotiating the national medicine price. Various methods and 'baskets' of reference countries are used. ERP is also called 'external price benchmarking' or 'international reference pricing'. [pp.2-3]

**What is the policy used for?**

Some countries use ERP to regulate the retail prices of medicines sold to the public. In this case, ERP is applied at the point when the company seeks authorization for marketing the product in the country. Other countries use ERP only to set prices of medicines that are included in the reimbursable list for social health insurance or the list of medicines covered by a public health system. In this case, ERP is applied as a condition for including the medicine in the list. The reference price may also be used as an explicit or confidential benchmark in price negotiation with the supplier. Japan uses ERP for adjusting the regulated medicines prices up or down over time. [p.3]

**How and where has it been implemented?**

ERP is widely used among high-income countries: 24 out of 30 OECD countries and 20 out of 27 European Union countries use some form of ERP. The WHO/HAI review identified 14 countries that reportedly use ERP and was able to obtain information from nine of these, predominantly middle income countries (Brazil, Czech Republic, Hungary, Iran, Lebanon, South Africa, Oman, and the United Arab Emirates). Use of ERP has been expanding over the past 10-15 years as the pharmaceuticals market has become increasingly globalized, replacing older cost-plus methods of price regulation in a number of countries. [p.19]

Most of the OECD or EU countries that use ERP restrict it to on-patent products, and some apply it only to products with new active ingredients. A number of middle income countries apply it to all medicines. Iran applies ERP only to imported on-patent medicines, using cost-plus pricing for locally manufactured products.

**Key aspects of designing an ERP system**

**Choosing reference countries:** Reference countries should have an adequate medicine regulatory regime for assuring product quality. Most ERP countries choose reference countries with similar per capita income to their own and countries in their own geographic region. The nine ERP countries surveyed for the WHO/HAI review used four to eight reference

countries. Transparent, up-to-date data on manufacturers' ex-factory prices must be accessible. Choice of reference countries also depends on policy objectives. Most countries have an objective of reducing prices or expenditure and so choose reference countries with relatively low prices. But some also have an objective of supporting innovation and so choose reference countries with a large pharmaceutical research base. In some countries, the selection of reference countries is subject to consultation with stakeholders or negotiation with the pharmaceutical industry. [pp.28-29]

**Calculation of the reference price:** The majority of countries use either the minimum or the average of manufacturers' ex-factory prices in the reference countries as the basis for calculating their ERP. Some countries adjust manufacturers' ex-factory list prices for factors such as estimated discounts or incentives offered in reference countries, or the difference between their nation's per capita income level and that of the reference countries. Some countries use additional criteria (such as the cost of existing treatment for the same condition) as a basis for setting the price or negotiating prices with suppliers. [p.30]

**Complementarity with other policies:** Countries that use ERP only for regulating prices of on-patent products often complement this with other policies for off-patent medicines such as pricing generics at a percentage below the originator brand price or cost-plus price regulation for locally manufactured generics. Some countries do not regulate the prices of off-patent medicines, but instead implement policies to promote price competition. Countries that use ERP only for regulating prices of medicines sold to the public, usually apply complementary methods for setting reimbursement prices paid by social health insurance agencies or public health systems such as internal reference pricing, competition for listing in the reimbursable list or formulary, and competitive procurement. [p.28]

**What institutional and technical capacity and information is required?**

Compared to other methods of price setting such as health technology assessment, ERP is a relatively less complex technical analysis and judgement. Like any form of price regulation, ERP relies on monitoring, inspection of pharmacies and enforcement capacity. Many low-income countries have limited capacity for pharmacy inspection and face constraints and delays in using law enforcement and judicial systems to ensure compliance with price regulation. [pp.24, 31]



### What specific challenges were encountered and what lessons can be learned?

There is a wide range of practice in how countries apply and enforce ERP. At one end of the spectrum are countries that apply a prescribed methodology for ERP underpinned by detailed, transparent regulation. Some countries use external audit to ensure regulations are followed correctly and transparently. Some countries reportedly apply the methodology strictly, refusing to authorize or reimburse medicines if the supplier is unwilling to accept the ERP-based price. At the other end of the spectrum are countries that use ERP as one of a number of methods for setting a benchmark that is used flexibly in negotiating prices with manufacturers. There is some evidence that where a manufacturer is in a monopolistic position, they may refuse to supply a medicine until the country agrees to exempt them from strict application of the reference price and negotiate a higher price (1). There are also cases where countries apply periodic unilateral or negotiated price adjustments or price cuts on top of ERP to deal with issues such as exchange rate movements or fiscal pressures. (p.19)

It is often challenging to obtain reliable price data from reference countries. Many countries rely on the manufacturer to supply price information in reference countries, with regulations that allow them to impose penalties for provision of false information. However, in many countries, manufacturers give confidential discounts to wholesalers and retailers from the ex-factory posted price, and information on the effective price actually transacted is not available. In some countries (including Spain, UK, France, Italy, Hungary, etc.), manufacturers pay back to the government various rebates or refunds, such as discounts on sales, refunds of excess profits or risk-sharing payments if sales exceed agreed levels. These practices make it very difficult for countries to verify if manufacturers have provided accurate information. If the ERP methodology makes no adjustment for discounts and rebates, it can lead to prices that are substantially higher than actually paid in the reference countries. Some countries report problems of delay in issuing pricing decisions because of delays in obtaining price data from some reference countries. If the ERP is set by simply omitting these reference countries, there is scope for manufacturers to manipulate the ERP by deliberate delays in launching products in low-priced reference countries. (pp.11-13)

### Effects of ERP, internal reference pricing and generic competition in Slovakia (3)

*Slovakia uses ERP to set a ceiling on patient prices for imported on-patent medicines as a condition of including them in the reimbursable list for social health insurance. Until 2005, it set the ERP at 10% above the average of the 3 lowest ex-factory prices in 9 reference countries: the country of origin plus 8 specified EU countries, including some with relatively high prices. If a reference country had not yet established a price for the product, this country was simply omitted. These policies left room for companies to launch their products early in Slovakia at a relatively high price before launching in lower priced reference countries. As a result, Slovakia's ERP prices were high compared to countries with similar income levels in the region. In response to these problems, Slovakia has since changed its ERP, currently referencing to all 26 other EU member states. For off-patent medicines and medicines which have a similar chemical structure and therapeutic effect, Slovakia uses internal reference pricing and competition among generic equivalent products. This results in effective price control.*

### How has the policy been monitored and evaluated?

There are few published studies of ERP. The WHO/HAI review identified 21 studies, of which 13 were opinion pieces; four used theoretical analysis and only four studies used databases or surveys. Most studies of ERP are from OECD or EU countries. Both the OECD and EU have undertaken studies of pharmaceutical pricing and other pharmaceutical policies among their member states. Very little information of any kind is available about ERP in middle- and low-income countries. South Africa has established a price monitoring committee with participation of its competition authority, health and pharmaceutical authorities.

### What effect does the policy have on prices and availability?

The effect of ERP on pricing depends on the selection of reference countries and the price calculation method (minimum versus average price). Including the country of origin of the product as one of the reference countries tends to lead to higher ERPs. Some countries only use a country as a reference if that country has included the medicine in its list of reimbursable medicines, which may lead to lower ERPs. If there is only one reference country, often this is a high-price, non-price-control country.

Some countries surveyed for the WHO/HAI review claim that ERP resulted in price reductions.



[as much as 30% in some cases], but no evidence from monitoring data or more rigorous analysis is available to support these claims. A wide range of price and per capita expenditure levels exist among OECD countries that use ERP, which is expected because of differences in policy objectives and implementation, and use of other price-setting mechanisms alongside ERP (1). Italy introduced ERP using UK, France, Germany and Spain as reference countries, then abandoned it in 2001, reportedly because it was found to be ineffective in containing public pharmaceutical expenditure (2). (pp.11-13, 20)

### Are there risks associated with the policy?

There is no clear theoretical rationale for choosing a particular set of reference countries or methodology for calculating the reference price. Because of this, there is a risk that when the ERP system is designed, non-transparent negotiation with industry may lead to choice of reference countries and methodology for ERP which results in higher prices than could have obtained without ERP. This risk can be reduced by transparent and open processes for designing the ERP regulations. This will mean clarifying policy objectives and agreeing in advance on fair and reasonable principles for choice of reference countries and methods for calculating the ERP. For example, some countries may agree on an aim of paying no more than countries with similar income and fiscal capacity. Alternatively, low and middle-income countries may agree on the principle of paying less than richer countries while ensuring that prices are sufficient to cover the costs of medicines with assured quality.

One alleged negative effect of ERP is that it may lead to delays in product launch. Another potential negative consequence of widespread use of ERP is convergence in international prices because companies may be unwilling to offer lower prices in any country that might be used as a reference. For example, one study found that prices for some medicines were kept high in Germany and New Zealand, even though this reduced market share, in order to ensure a higher ERP in countries that used Germany and New Zealand as references. This phenomenon could be expected to lead to convergence of prices at a higher level than companies would otherwise be willing to offer to low-income countries, which on average have lower medicine prices than high-income countries. Another potential negative effect of ERP is that it may lead companies to respond by reducing price transparency, for example, by offering confidential discounts or rebates to reference country governments. There is some evidence of delayed launch in low-price countries, some evidence of convergence in international prices for new medicines, and documentation of increased use of non-transparent rebates and

discounts. However, this evidence is not specifically attributable to ERP and may also be due to other factors. Delayed entry may occur in countries where low prices are due to other forms of price control or to other factors that make some low-price countries unattractive (for example, small market size or high costs of doing business). Price convergence and use of confidential discount agreements may be a response to parallel trade as well as to ERP. (pp.22-23)

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## Value in Pharmaceutical Pricing

Paris V, Belloni A. 2013

OECD report about value-based pricing

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## EXECUTIVE SUMMARY

1. The objective of this study is to describe how OECD Member Countries refer to “value” when making decisions on reimbursement and prices of new medicines. The study scrutinised reimbursement and pricing policies in 14 OECD countries. In addition to describing the formal differences in how value-based pricing is applied in these countries, a more detailed examination of the decisions made about 12 products brought to the market between 2005 and 2011 was conducted. These products were chosen to illustrate differences across countries in how value is assessed and how this might affect reimbursement decisions and pricing outcomes.
2. Ideally, information on prices actually paid by purchasers is needed to understand fully the impact of “value-based” reimbursement and pricing policies. Unfortunately, price information is not available for a number of products in our sample. Reliable price information was available only for a small number of products used in ambulatory care with list prices likely to correspond to actual prices. The project also tried to collect information on the use of all products, but such information was often not comparable or simply not available.
3. Despite these data limitations, this report does answer some of the questions about how value-based pricing works in practice, and how much different conceptions of ‘value’ actually matter.
4. The first conclusion is that the types of health outcomes considered by assessment bodies to inform decisions on reimbursement have more in common with each other than differences. For example, all countries prefer final endpoints to surrogate markers to assess health outcomes where available. Countries using economic evaluation explicitly consider utility for patients when assessing incremental cost-utility ratios, while other countries do not systematically do so. This difference might be expected to have an impact on reimbursement decisions, price levels and relative prices of different categories of products. However, from the sample of countries and products scrutinized, it was not possible to identify such an impact.
5. Second, countries using economic evaluation are more sensitive to uncertainties attached to health outcomes or costs. They rejected funding applications on grounds of uncertainty more often than countries without economic evaluation. This may be due to the formal presentation of sensitivity analysis in economic assessments, which raises awareness of decision-makers.
6. Third, several countries have chosen a societal perspective to evaluate health technologies (e.g. Sweden and Norway). While this choice could, in principle, have a big impact on prices paid for products with a big social impact (such as increasing labour market productivity), in practice there is little evidence that it makes much difference.
7. Fourth, one of the objectives of value-based pricing is to reward innovation. This is mainly assessed through the added therapeutic value of new medicines over existing treatment alternatives. If assessment bodies confirm that a drug has some added therapeutic value, this influences the analytical method used in economic evaluation or the rules applying to price regulation in countries which do not use economic evaluation. Payers are in principle ready to pay a price premium or to allow incremental costs for an innovative product. However, establishing a clear link between the level of innovativeness and the price

premium seems impossible. Assessing the implied value of a QALY is also difficult since there is little evidence of consistency across products.

8. Fifth, improvements in the process of care, without a direct impact on health, may have sometimes resulted in a higher price being paid for new products, although the evidence is not clear. By contrast, no evidence was found that innovation “beyond therapeutic value” is considered *in practice* to make reimbursement or price decisions.

9. The sixth conclusion is that the study confirmed that disease severity and rarity receive particular attention, justifying higher prices or incremental cost-effectiveness ratios (ICER) in case-study countries. While some countries have explicitly defined criteria that should be taken into account (e.g. NICE with the end-of-life criteria), others do not have pre-defined rules. Countries that do not use economic evaluations are also more likely to accept high prices in similar circumstances.

10. When medicines are approved for several indications which display very different cost-effectiveness ratios, countries have adopted different attitudes. The seventh conclusion is that most often, the price of a medicine is unique, set at market entry, and countries make a “yes or no” decision for each new indication. The price may be reviewed (always downward in our sample) when a new indication is funded. In some occasions, product-specific agreements have been used to permit price discrimination across market segments defined for each indication.

11. Beyond these conclusions, it should be noted that price is not the only component of value. Very often, decision-makers have to trade-off prices against potential market sizes and are willing to extend indications in exchange for a lower price as long as benefits for patients are clearly shown. Negotiations of this type seem more likely to occur in systems not using a formal evaluation process.

12. Finally, international benchmarking is still widely used in price regulation, with several implications. The first is that it does not seem completely compatible with value-based pricing. The second is that the future implementation of value-based pricing in the most referenced countries will have an impact in other markets, which is difficult to predict at this stage.



# Differential pricing of pharmaceuticals: Review of current knowledge, new findings and ideas for action

Yadav P. 2010

Report of the MIT Zaragoza International Logistics Program

## Executive Summary

Adapting drug prices to the purchasing power of consumers in different geographical or socio-economic segments could potentially be a very effective way to improve access to medicines for people living in low and middle-income countries. A well-implemented differential pricing system could also lead to increase in sales for pharmaceutical manufacturers.

The pharmaceutical industry has been cautious about significantly changing its pricing models, despite the theoretical appeal of differential pricing and its success in improving access to medicines in low- and middle-income countries. This reluctance is caused mainly by concerns that differential pricing could erode profit margins in lucrative high and middle-income markets and high distribution channel markups in low income countries could dilute much of the benefits of differential pricing to poor end-patients.

Recent trends, however, are prompting the pharmaceutical industry to pay more attention to differential pricing, such as economic and demographic growth in some low and middle-income markets, which has increased the potential market size of many low and middle income countries; greater recognition by the pharmaceutical manufacturers and their investors of the social responsibilities; stronger global advocacy for access to medicines, and growing competition from generic manufacturers in emerging markets. Differential pricing allows pharmaceutical companies to signal that their pricing policies are socially responsible and consistent with their obligations to society and not just geared towards maximizing profits. In addition, differential pricing on select drugs opens opportunities to serve low and middle-income markets and creates economies of scope for pharmaceutical companies.

A review of the existing literature on differential pricing and analysis of successful and unsuccessful examples of such pricing reveal that it may lead to overall welfare benefits only when the overall sales increase as a result. The analysis also suggests that social welfare is enhanced when differential pricing opens new markets for pharmaceutical companies in countries where the affordability for the drug is significantly lower than the prevailing price in existing markets. Whether the benefits of differential pricing accrue more to the pharmaceutical company or to the patient/payer depends on the elasticity of demand and the market structure.

It is important to note that differential pricing is not a panacea to ensuring access. For patients with affordability levels lower than the marginal cost of manufacturing, donor subsidies and government support will continue to be required.

Despite some evidence that differential pricing of pharmaceuticals can benefit manufacturers and poor countries without adversely affecting higher income countries, the widespread and systematic use of such pricing has been limited to vaccines, contraceptives, and antiretrovirals (ARVs) mostly in low income countries.

Differential pricing of ARVs between high, middle and low-income markets, however, has raised complicated economic, legal, and supply chain challenges. The lure of getting prices paid by low income countries has raised substantial legal and political tensions between pharmaceutical companies, middle income country governments and non-governmental organizations. The three-tiered pricing structure used for ARVs has been the subject of intense debate in middle-income countries. Some of these countries have vast income inequalities and the average



income level does not reflect the true issues that impede access. The people in these income segments, the civil society groups that represent them, and the political support system together push for obtaining low-income prices for these population segments in lower-middle or middle-income countries.

In the case of vaccines, most now have a three-tiered pricing structure with fully loaded market prices charged in rich countries, low prices in countries belonging to the Global Alliance for Vaccines and Immunization (GAVI), and intermediate prices in middle-income countries. However, the practice of charging higher prices in middle-income countries than in the poorest countries has been contentious. Firms argue that middle-income countries, especially upper-middle-income countries such as Brazil, have substantially greater capacity to pay for vaccines than do GAVI countries. Middle-income countries argue that their populations include many poor people and the prices they pay should be not too far from what the least-developed countries are paying.

More research is required on how differential pricing can be expanded to include all essential medicines for low and middle-income countries and how fair, affordable prices should be determined. Further research is also required to understand the impact of buy-side market structure on the social welfare impact and the operational feasibility of differential pricing.

Despite its theoretical appeal and some notable successes, the use of differential pricing as a tool to improve access to medicines is not widespread. The primary causes include risks of physical arbitrage (lower priced product flowing back to the high income markets); risks of eroding margins in high income market segments due to external referencing (where countries compare the prices for new products against those prices paid by other countries within the geographical region or income class); poor knowledge of demand and supply structures; and a buying market structure that works against the poorest segments of the population.

Based on the analysis conducted for this report as well as an assessment of the existing literature, several strategies are recommended for mitigating the risks associated with differential pricing.

To help pharmaceutical firms avoid political pressure from middle income countries to lower drug prices and to increase sales in those markets, firms could use intra-country differential pricing. In lower middle and middle income countries different socio-economic segments of the population seek treatment and obtain medicines from different channels, with wealthier patients seeking treatment in channels different from their poorer counterparts. This provides a natural wedge that can be leveraged for charging different prices in the different channels and reaching specific segments of the population at price points that they can truly afford. Another natural wedge that can be leveraged for intra-country differential pricing is the urban-rural income divide in developing countries.

To prevent physical arbitrage from one channel to another within a country, firms could work closely with global agencies that have a strong reputational risk from cross channel arbitrage in the drugs they finance. This would allow them to share the risks of arbitrage and collectively create strategies such as enhancing top to bottom visibility in the supply chain to counter diversion across channels. In addition, firms could develop contractual agreements with public or private distribution channels who primarily serve the poor population segments. The contractual

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agreements would agree to provide lower priced products in return for ensuring that the product is only used in the market for which it is intended.

To avoid the problem of formal or informal external referencing, firms could nudge countries to use pharmaco-economic assessments instead of reference pricing and increase local context-specific health outcomes research.

Implementation of differential pricing will require better information about markets, political will, and commitment from pharmaceutical companies and developing country governments.



# Challenges and opportunities in improving access to medicines through efficient public procurement in WHO European Region

Ferrario A, Kanavos P, Humbert T, Iwamoto K, Bak Pedersen H. 2016

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## Key findings from the consultation

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The following topics were discussed during the WHO consultation with Member States. This section sets out a summary of the main points raised.

### **1. Analysing spending on medicines in hospitals – what can be achieved? How can this information be used proactively in developing specific approaches to procurement for specific categories of medicines?**

The consultation confirmed that countries' public procurement practices are very different among European countries. Some countries have developed public agencies for procurement that negotiate and manage the introduction of new high-price medicines into the hospital sector. In these countries, clinicians are involved in the process of development of the tender document to ensure alignment in the introduction, management and use of medicines in the inpatient sector and to foster their responsible use. Analysing spending on medicines in hospitals is an important tool in these cases. The focus is on efficiency and reduction of waste, sustainable access to innovation and efficient use of public resources.

Other countries have limited control over what products are procured and used in their hospital sectors; there is limited or no collaboration between hospitals on pricing, procurement and/or fostering efficiency and reduction of waste linked to use of public pharmaceutical expenditures.

Whether or not countries have public responsibility for procurement for the hospital sector it is considered important to analyse both hospital spending on medicines and the market to obtain efficiency, best prices and supply sustainability.

It seems likely that analysing spending on medicines in hospitals can be strengthened in many countries through voluntary collaboration by relevant partners. Such analysis would help to identify opportunities and efficiency improvements that may provide room for manoeuvre and facilitate sustainable access to medicines.

### **2. Practical steps to develop an international/national tender for new medicines for hospitals and the use of various procurement tools as contractual modalities**

With an analytical approach to procurement of medicines, procurement experts can benefit from collaboration with other countries' experts. Some countries in Europe face challenges owing to their size, language and geographical position, but some of these challenges could be overcome and this should be explored further by strengthening subregional collaboration.

Depending on the products, different tender procedures can be considered. Price should not be the only criterion used to award a supplier a contract: supply security and the concept of a healthy market should also be considered. Countries may also wish to consider further analogue competition, as this has proved useful. Developing specific procurement strategies can be helpful in obtaining efficient results; it was suggested that there should be more focus on joint development of procurement strategies for specific priority medicines to facilitate fair pricing and sustainable access to new high-price medicines.



**3. Stakeholder analysis before moving to centralized procurement: exploring possible partnerships, benefits and challenges. How to develop strategies that involve partners, inform stakeholders and prepare for any negative reactions.**

Many stakeholders have a role in the procurement process and the power and influence those groups have varies depending on the country. It is essential, however, to conduct a stakeholder analysis when a country decides to move from decentralized to centralized procurement. The potential benefits of voluntary centralized procurement are many, including enhancement of the strategic procurement capacity. Nevertheless, planning is very important and stakeholder analysis is essential to elucidate challenges and opportunities.

**4. How can improved transparency (nationally as well as through international cooperation) support strategic procurement?**

Price transparency could have benefits for many countries and seems relevant for public procurement of medicines. Sharing non-price information is also important to increase transparency. Countries in Europe are willing to enhance national and international cooperation; increasing transparency is an important commitment to good governance and will be an important element in future work on fair pricing.

**5. Prerequisites for preferred contracts with supplier to ensure value for money in the outpatient sector**

Price should not be the only criterion to award a supplier a contract: many other technical requirements should be taken into consideration. Having more than one supplier is essential for a healthy market, and use of separate contracts for distribution of medicines is a relevant tool to consider. To ensure supply, contracts should include guarantees. Different contract modalities are available and should be used according to the specific situation.

## **Review 6: Health Technology Assessment in Medicine Pricing and Reimbursement**

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### **Policy brief #6 Pharmaceutical Pricing Policies and Interventions**

WHO/HAI. 2011/2014

WHO/HAI review about HTA for medicines worldwide: a mapping exercise and evidence about impact





## Pharmaceutical Pricing Policies and Interventions

POLICY BRIEF NUMBER 6

# THE ROLE OF HEALTH TECHNOLOGY ASSESSMENT IN MEDICINE PRICING AND REIMBURSEMENT

As part of the joint World Health Organization (WHO)/ Health Action International (HAI) Project on Medicine Prices and Availability, a series of in-depth reviews have been published on pharmaceutical policies and interventions that may improve medicine availability and affordability. This policy brief summarises the key points from the review on the role of health technology assessment (HTA) in medicine pricing and reimbursement with a focus on its use in low- and middle-income countries (LMICs). The review included a systematic literature review and a description of policy processes and requirements.

Page references to the review paper are given in parentheses.



### WHAT IS THE BASIS FOR THIS POLICY BRIEF?

WHO/HAI Review Series on Pharmaceutical Pricing Policies and Interventions. Working paper 6: *The role of health technology assessment in medicine pricing and reimbursement* by Patricia Whyte and Cameron Hall, Deakin Health Economics, Deakin University, Australia. [www.haiweb.org/medicineprices/policy/index.html](http://www.haiweb.org/medicineprices/policy/index.html)

## SUMMARY CONCLUSIONS

### What are the main advantages of HTA?

HTA can increase value for money from scarce public resources and help to control medicine expenditure.

### What are the main disadvantages of HTA?

It is costly to conduct and requires strong technical capacity. Decision-makers must have skills to interpret and apply HTA findings. The pharmaceutical industry, medical specialists and some patient groups for particular diseases often oppose HTA policies because they fear it may restrict marketing of, and access to, costly new medicines.

### Is HTA appropriate for regulating all medicine prices?

HTA is most appropriate for innovative new medicines. For medicines which are off-patent or have close therapeutic substitutes, other policies may be more efficient.

### Is HTA appropriate for all countries?

Low-income countries with very limited capacity and countries that face major challenges of lack of transparency in decision-making on medicines reimbursement are likely to face difficulty implementing HTA for medicines effectively. Use of international guidelines and model essential medicines lists can help such countries to incorporate HTA in their policies.

### Are there any complementary policies that should accompany HTA?

Other policies can put downward pressure on prices for off-patent medicines and medicines with close therapeutic substitutes, including competitive tendering and therapeutic reference pricing. Policies to encourage doctors to prescribe formulary medicines and follow evidence-based guidelines are needed to complement HTA.

### Are there any key pre-requisites for implementing HTA?

Capacity for HTA in LMICs should be established early and supported; prerequisites and barriers are extensive but not insurmountable and must be considered as HTA processes are developed.



### What is the policy?

Health technology assessment (HTA) is a multi-disciplinary policy analysis of the medical, economic, social and ethical implications of development, diffusion, and use of health technology, including medicines, vaccines, medical devices and interventions. HTA for medicines typically uses clinical, pharmacological and pharmaco-economic analysis to assess whether a new medicine provides any additional benefit compared with current practice and at what additional cost, and may recommend that a medicine be used for specific indications or patient sub-groups. HTA often quantifies fiscal and population health impacts of increased use of the technology. HTA seeks to synthesise research evidence and develop recommendations for decisions by policy-makers, managers and clinicians. (p.1)

### What is the policy used for?

HTA findings can be used to prioritise health care expenditure, increase value for money and control health expenditure. HTA of medicines is widely used in Organization for Economic Cooperation and Development (OECD) countries to inform the selection of medicines for national, regional or hospital drug formularies and the selection of medicines for reimbursement by health insurance systems. In many countries and global and national health organizations, HTA is used as an input into the development of evidence-based clinical guidelines and into advice to prescribers. A few countries use HTA in negotiation of medicine prices. (pp. 7-8) In the case of medicines, HTA is usually carried out after the medicines regulatory authority has assessed quality, safety, and efficacy. The subsequent use of the HTA findings to inform decisions about formularies, pricing and reimbursement of medicines is usually a separate process from the assessment itself. There is considerable variation in how countries use HTA to inform policy, management and clinical decisions. (p.2)

### How and where has it been implemented?

Australia was the first country to require companies to submit economic data to support applications for new pharmaceutical products to be reimbursed through its pharmaceutical benefits scheme (PBS) in 1993. Since then, most OECD countries have followed suit and now require HTA as part of their decisions on the reimbursement of new medicines. (pp. 7-8) Countries typically only mandate HTA for new products that are on-patent, not for new generics. Where countries use HTA to develop and update clinical guidelines, the assessment also reviews new evidence on existing medicines and other therapies.

Interest in HTA has expanded internationally and now a number of middle-income countries have established HTA agencies or commission HTA from

academic and other institutions, including Argentina, Brazil, Chile, China, Colombia, Croatia, Malaysia, Mexico, Poland (now a high-income country), South Africa, Thailand, Turkey and Uruguay. A number of these countries have introduced HTA as part of their decision processes for medicines reimbursement policy. But HTA is developing at uneven speeds across countries and the role of HTA differs from country to country. (p.12) It seems that many LMICs have no HTA processes, and information is hard to obtain about the development of HTA in LMICs. Many LMICs draw upon guidelines developed by global health institutions that are informed by HTA, such as the WHO model essential medicine lists. (p.22)

### Key aspects of designing HTA processes for medicines

An international working group proposed the following key principles when designing HTA processes: consideration of evidence and outcomes, consideration of the full societal perspective, generalisability of findings, timely assessments, transparency of the HTA process and transparency of the link between HTA findings and decision making. (1) (p. 8)

Legislation is normally necessary to require HTA processes for defined categories or types of new medicines before decisions are made to include them in a national formulary or list of reimbursable medicines. The legislation should clearly define what is expected in HTA by referencing guidelines, how the analysis will be evaluated, decision-making criteria, roles and composition of various committees that should be established, whether the opportunity exists to appeal if unsuccessful, requirements to make the findings of the evaluation available to the public, and fees that would be levied for each application. It is good practice for legislation to include provisions to ensure that participants in HTA and subsequent decisions do not have any conflict of interest. Legislation should allow for decisions of the national organisation to be challenged under certain circumstances and also for recourse against pharmaceutical suppliers if they have not met contracted terms. (p.19)

The manufacturer usually lodges the submission with the national organisation responsible for managing the national formulary. The national organisation then assigns the submission for evaluation, which may be carried out in-house or outsourced to an organization with suitable expertise to conduct independent evaluation. A multidisciplinary team including a health economist will conduct the evaluation, which is then presented to a committee of experts for discussion and recommendation to accept or reject (or defer pending future data) the pharmaceutical for listing on the formulary. (p.16)



### What institutional and technical capacity and information is required to implement the policy effectively?

HTA requires expertise in a number of areas including health economics, biostatistics, pharmacology, epidemiology and a range of fields of clinical medicine. It is vital to have experts with the ability to critically review and apply statistics for the proper interpretation and application of economic evaluations. LMICs need to offer competitive salaries or other incentives to attract and retain staff with the necessary expertise. A 2001 survey of HTA of pharmaceuticals in 11 OECD countries found that the staffing of these agencies ranged from 5 to 23 full-time positions, depending on the number of assessments to be conducted and whether external consultants were used. [2] The head of the HTA agency is usually appointed by the Ministry of Health. Most countries use external consultants or outsourcing to academic or other research institutions for conducting HTA. It is also important for decision-makers who consider the HTA reports and recommendations on formulary listing or pricing to have the skills to objectively assess the evidence presented to them, or to have access to policy advisers with these skills. However, some studies of country experience suggest that technical expert capacity can be built up over time by making the technical requirements less stringent initially. [pp. 16-17]

The resources to establish an HTA organisation may have to come from government initially. However, the operating costs could be funded at least in part through a submission fee applying to manufacturers. [p.16]

Sharing of HTA guidelines and information across countries can reduce the burden on individual countries. However, the adaptation of HTA across countries is a key concern, particularly for LMICs. Some HTA information will be relevant in every setting, for example, evidence from systematic literature reviews and evidence from randomised controlled trials regarding the effectiveness of an intervention. However, factors such as the epidemiological profile of disease, models of clinical practice, relative prices and unit costs, the availability of healthcare resources and budget constraints, as well as the choice of health benefit, comparator, comparability of treatment patterns and populations, are more country-specific and hence may limit the generalisability of results. While the technical aspects of best practice within HTA, such as transparent reporting of methods and findings, can be applied across countries of all economic levels, other aspects of HTA are best developed specific to each setting. However, countries with limited HTA capacity can prioritise assessments based on the practice of high-income countries (HICs) where HTA is well established. For example, if an HIC finds that a

particular technology is not cost-effective, it will likely not be cost-effective in an LMIC setting either. [pp. 19-20]

### What specific challenges were encountered and what lessons can be learned?

Countries have encountered many barriers to the implementation of formal HTA processes, including shortage of expertise; timeliness of availability of necessary information; linking the different participants and organizations involved in HTA and subsequent decisions, including pharmaceutical companies, experts, researchers, and decision makers; lack of decision-maker capacity; limited acceptance of external data; transparency and comprehensible communication of HTA reports and decisions; and incentives to use HTA evaluations. These barriers are substantial, but a growing number of countries have demonstrated that they can be overcome. The evidence from the literature search addresses possible solutions to each of these challenges. A review of how HTA has evolved in several European countries over the past decade found that countries have generally strived to modify their methods to improve the impact of assessments on policy and practice, meet national objectives and the various needs of stakeholders, and achieve greater transparency, legitimacy and relevance. [3] [pp. 9-10,21] This suggests LMICs initiating HTA should plan to review and improve their HTA processes and implementation over time.

The pharmaceutical industry perceives HTA as a barrier to gaining market access. Consequently, the industry is typically resistant to the introduction of HTA before medicines are reimbursed. Companies may have to employ new staff or contract a consultancy at considerable expense to prepare submissions to the HTA agency. Public reimbursement of a medicine, however, offers a strong incentive for industry to cooperate and the skills requirement is not insurmountable, particularly for multinational companies which are the main producers of new medicines requiring HTA. [p.17]

Doctors, particularly specialists, may also have concerns about the risk that HTA may restrict their ability to prescribe new medicines if rejected for public reimbursement. Patient groups may share the same concerns. Early and meaningful consultation with specialists in the field before decision-making is necessary to address this issue. Consultation with patient and consumer groups before decision-making, or the establishment of a forum, can ensure the needs and experiences of patients are well understood before decisions are made and can help to ensure effective communication of HTA findings. Effective participation of civil society organisations can also provide a check or balance for the organisation that makes funding decisions based on HTA.



However, some patient groups are fragmented and/or source their funding from interested pharmaceutical companies. (p. 18)

### How has the policy been monitored and evaluated?

There is little comparative and quantitative evidence on the effect of the application of HTA on medicine prices, availability and affordability. This is especially true in the setting of low- and middle-income countries. There is a body of descriptive evidence on the role of HTA and its implementation which enables some tentative conclusions to be drawn on the likely impact that HTA would have. As one commentator noted, whereas the last 10 years have been well spent on building the HTA infrastructure and evidence base, the next decade should focus on ascertaining outcomes. (p.22)

### What effect does the policy have on prices and availability?

There is some evidence that HTA can be used to manage medicines expenditure growth effectively while maintaining availability, when it is combined with other tools such as restricting reimbursement to pharmaceuticals on a national formulary. (p.21)

Only a small number of HICs appear to use HTA for negotiating value-based prices for innovative new medicines, including Australia, Canada, the UK, France and Germany. In these countries, the negotiation of the reimbursement price involves wider considerations in addition to HTA. One study compared the effects of using HTA in price negotiation with using therapeutic reference pricing for selected groups of medicines in four countries that had used one or both policies. [4] HTA did not result in any clear pattern of impact on pricing. Reference pricing was found to be effective in lowering prices of medicines that are therapeutically equivalent in cases when there was a big difference in prices among equivalent medicines – for example when one medicine in the group went off-patent and attracted competition from generics. HTA is, in theory, a superior method for obtaining value for money because it addresses not only price, but also the appropriate indications for the use of the medicine and the relation between additional value and additional costs. However, conducting HTAs is more costly than reference pricing, so the most efficient approach might be a combination of both policies. (p. 39)

### Are there risks associated with the policy?

Even high-income countries with strong HTA capacity still face challenges, generally relating to the evidence presented. One review of HTA decisions for medicines in the UK, Canada and Australia found that significant uncertainty around clinical

effectiveness, usually resulting from inadequate study design and the use of inappropriate comparators, was a key issue affecting decisions the countries made to reimburse new medicines. [5] As well, the results of the evaluation process in the different countries appeared to be influenced by the context, agency processes, ability to engage in price negotiation and perhaps differences in social values. It is expected that this would also be true in LMICs. (pp. 11-12)

Reimbursement decisions often consider information other than just cost-effectiveness results, but the full range of decision criteria leading to a reimbursement price is often not transparent. Transparency is vital to convince stakeholders that the decision is made based on sound and consistent principles. This is of particular importance in countries – both LMICs and higher income countries – that face challenges in managing medicines policies arising from conflict of interest and corruption. (pp. 9-10) Clear and objective criteria for decision-making and publication of HTA recommendations and reasons for reimbursement decisions can contribute to transparency of the process and stakeholder and public acceptance. (pp. 17-18)

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## Managed entry agreements for pharmaceuticals: The European experience

Ferrario A, Kanavos P. 2013

Overview about managed entry agreements in Europe

### EXECUTIVE SUMMARY

#### **Background**

Stretched health care budgets, increasing availability of potentially life-saving high-cost drugs and increasing patient expectations, mean that manufacturers seeking inclusion in reimbursement lists need to demonstrate that their drugs can provide additional benefit in relation to current therapies and value-for-money in order to obtain coverage. Data and the overall evidence base available at registration are often insufficient to accurately estimate the clinical and cost-effectiveness of a drug in clinical practice or its budget impact in real life. Uncertainty, due to lack of information on effectiveness, may delay reimbursement decisions and patient access. Delays together with the threat of non-inclusion in positive lists may dis-incentivise industry from investing in high-risk areas with low market potential such as orphan drugs.

Against this background, formal arrangements between payers and manufacturers with the aim of sharing the financial risk due to uncertainty surrounding the introduction of new technologies have been developed and introduced in order to enable access to new medicines. These agreements can take different forms, including price-volume agreements (PVAs), outcome guarantee, coverage with evidence development (CED), and disease management programmes. A variety of names have been used to describe these schemes (e.g. risk-sharing agreements (RSAs), performance-based agreements (PBAs), patient access schemes (PAS), etc.), which have been recently summarised with the concept of “managed entry agreements (MEAs)”.

#### **Objectives**

The aim of this study is threefold. First, to collect quantitative information on MEAs such as the number of agreements by therapeutic area and the types of agreement implemented. Based on this information draw some conclusions on the kind of uncertainty (related to budget impact, clinical and cost-effectiveness or both) payers are trying to address. Second, to develop a taxonomy for MEAs which will be used to classify the identified agreements. Third, to assess MEAs’ ability to address uncertainty, maximise effective use of technology, limit budget impact.

### **Methods**

Data on MEAs implemented in the EU were collected between October 2011 and January 2012 using an online survey developed by EMINet.

Further insights and materials were obtained during the meetings and interviews with drug reimbursement authorities, industry and patients representatives.

### **Results**

Three-quarters (75%) of all the agreements in the study countries aimed to address budget impact, either alone (42%) or in combination with cost effectiveness (16%), use (15%) or both (2%). At country level, two main trends seem to emerge. In some countries, Italy, Portugal, Lithuania, the Czech Republic, and Belgium there was a strong focus on budget impact. While in others, Sweden, the Netherlands and the UK, cost effectiveness seems to be the driving force when deciding to engage in a MEA.

The most common features of MEA across countries were PVAs (40%), followed by requirement for data collection (29.4%), and limited access to eligible patients (12.6%). PVAs are widely used in Italy, Portugal, and Lithuania; data collection is a common requirement in Italy, the Netherlands, the Czech Republic and Sweden. Further, Italy, the Czech Republic and Belgium, limit access of certain medicines to eligible patients in an attempt to manage budget impact and use.

In terms of therapeutic groups, antineoplastic and immune-modulating agents represented 37.3% of all the MEAs implemented in the study countries, followed by alimentary tract and metabolism 16.5% and nervous system 9.8%. All member states apart from Sweden (only one MEA for ATC-L vs. 3 MEA for both ATC-B and ATC-N) the greatest proportion of agreement involved ATC-L drugs.

### **Discussion**

Managing budget impact is one the main objectives of MEAs in Belgium, the Czech Republic, Italy, Lithuania, Portugal, and the UK. This is reflected in the design of MEAs in these countries which includes features of PVAs, budget caps, and a compensation mechanism in Belgium, limited access through specialised healthcare centres in the Czech Republic, PVAs, discounts and conditional treatment continuation in Italy, PVAs, payback, and expenditure cap in Lithuania, PVAs in Portugal PVAs, and discounts, dose capping, initial free doses in the



UK. Sweden takes a more indirect approach by requesting the manufacturer to submit utilisation data to TLV which will be used at the end of the conditional reimbursement period to update the reimbursement decision.

There are two main ways to address uncertainty relating to clinical and/or cost-effectiveness. The first is to grant reimbursement for a limited time period during which additional evidence on the drug effectiveness will be collected and to update the reimbursement decision afterwards based on the new cost-effectiveness results. This model is used in the Netherlands, Sweden and Portugal. The second way is to decrease the price or to limit utilisation so that the cost-effective ratio is improved because of lower costs. Discounts are very common in the UK as part of patient access schemes while Italy uses a combination of discounts, payment-by-result and conditional treatment continuation to improve cost-effectiveness. However, this option does not address the underlying issue of uncertainty in cost-effectiveness unless linked with data collection which is intended for updating coverage decision.

The main strategy used to optimise utilisation is to limit prescribing and reimbursement to specific therapeutic indication and to those patients sub-groups who are most likely to benefit. The instruments used include limiting prescribing to specialised healthcare centres, use of biomarkers, and physician certification that the patient meets the eligibility requirements together with monitoring. The Czech Republic for example limits access to specific patient subgroups and to specialised healthcare centres. In Italy, patients eligibility is monitored through the registries and physician are request to certify that a patient meets the prescribing requirements in order for him to obtain the drug at the pharmacy.

### ***Conclusions***

European countries are using a variety of instruments to tackle uncertainty arising from lack of information about budget impact, cost-effectiveness, use in real life, and access. Despite the non-negligible number of agreements implemented, little information is available on the impact of these schemes and whether they are meeting their objectives. Moreover, the little amount of information available in the public domain is hampering cross-country learning and the ability of patients to engage in the process.

Previously proposed taxonomies do not well suit the reality at country level, where complex agreements with financial and health outcomes features are implemented. While there is



scope for improvement, the taxonomy employed in this study aims to address this issue by using a more versatile classification system which on one level focuses on the objectives countries are trying to achieve through MEAs and on a second level highlights and summarises the features of the implemented agreements. Further there is the need to agree on a common definition of MEAs and to define the boundaries between a MEA and a non-MEA.

## **Review 3: The Regulation of Mark-ups in the Pharmaceutical Supply Chain**

### **Policy brief #3 Pharmaceutical Pricing Policies and Interventions**

WHO/HAI. 2011/2014

WHO/HAI review about distribution remuneration worldwide: a mapping exercise and evidence about impact



## REGULATION OF MARK-UPS IN THE PHARMACEUTICAL SUPPLY CHAIN

As part of the joint World Health Organization (WHO) / Health Action International (HAI) Project on Medicine Prices and Availability, a series of in-depth reviews have been published on pharmaceutical pricing policies and interventions that may improve medicine availability

and affordability. This policy brief summarises the key points from the review on the regulation of distribution mark-ups, which included a systematic literature review and analysis of policy issues and options.

*Page references to the review paper are given in parentheses.*

### WHAT IS THE BASIS FOR THIS POLICY BRIEF?

WHO/HAI Review Series on Pharmaceutical Pricing Policies and Interventions. Working paper 3: *The regulation of mark-ups in the pharmaceutical supply chain* by Douglas Ball. [www.haiweb.org/medicine-prices/policy/index.html](http://www.haiweb.org/medicine-prices/policy/index.html)



### SUMMARY CONCLUSIONS

#### What are the main advantages of mark-up regulation?

If part of a comprehensive price regulation strategy, mark-up regulation can reduce prices and help to control expenditure. Mark-up regulation alone is unlikely to reduce prices.

#### What are the main disadvantages of mark-up regulation?

Poorly designed mark-up regulation can reduce availability of low-priced medicines and make rural pharmacies unviable. Those in the distribution chain can often find ways to evade

regulations or recoup lost profits by increasing other fees and prices.

#### What is the most appropriate form of mark-up regulation?

Regressive mark-ups and fixed fees can avoid perverse incentives to dispense high priced medicines and encourage dispensing of lower-priced generics.

#### Should mark-up regulation be applied to all medicine prices?

Selective regulation within a sector risks unintended effects on the availability of regulated products, but

countries may regulate mark-ups only for the public sector or only for reimbursement prices for social health insurance. Low-priced generics may be exempt.

#### Is mark-up regulation appropriate for all countries?

Countries that lack monitoring and enforcement capacity are unlikely to be able to implement mark-up regulation effectively.

#### Are there any complementary policies that should accompany mark-up regulation?

Additional policies may be needed to ensure medicine availability in remote areas. Promotion of generics and rational use can complement regressive mark-ups and fixed fees.

#### Are there any key prerequisites for implementing mark-up regulations?

Systems for consulting stakeholders, monitoring prices, sales and medicine availability are vital. Mark-up levels should be informed by intelligence on costs in the distribution chain.



Studies of medicine price components in low- and middle-income countries (LMICs) show variable and often high cumulative mark-ups, from 17%-84% in the public sector and 11%-6,894% in the private sector. The level of mark-ups among Organization for Economic Cooperation (OECD) countries also varies widely, from 2%-21% for wholesale mark-ups and from 4%-50% for retail mark-ups (pp.17,19). It is therefore important to find ways of improving efficiency and controlling costs in the pharmaceutical distribution chain.

### Defining distribution 'mark-ups'

Distribution mark-ups are the additions to the medicine manufacturer's or importer's supply price to cover the costs of wholesale and retail activities, including overheads, distribution costs and profit margins for wholesalers or other distributors and retailers. In traditional supply chains, the wholesale mark-up (expressed as a percentage add-on to the manufacturer's sale price) can be distinguished from the retail or pharmacy mark-up (expressed as a percentage add-on to the wholesaler's price or pharmacy purchase price). However, there can be diversity in how supply chains are organized, for example, pharmacy chains may carry out their own wholesaling functions, manufacturers may distribute directly to hospitals and pharmacies, or products pass through multiple wholesalers and distributors before reaching the retailer. Each adds a mark-up, leading to high cumulative mark-ups and prices. Importers also apply mark-ups. Because these mark-ups are applied early in the supply chain they will be compounded by the addition of distribution mark-ups, so their effect on the final patient price can be substantial. (p.2)

### Policy objectives

Price regulation usually has the objective of reducing medicine prices and containing pharmaceutical expenditure, while ensuring prices are sufficient to achieve availability and assure product quality. Mark-up regulation creates incentives and disincentives throughout the supply chain. Some forms of mark-up regulation seek to influence these incentives for policy purposes, for example, to promote dispensing of generics, to encourage price competition, to discourage non-transparent commercial practices that may be anti-competitive (e.g. volume rebates or bundling), or to support locally manufactured products. (p.14)

### What is the policy?

Mark-up regulation may be applied to the private sector and the public sector, and also used as part of a system for setting the reimbursement prices paid by social health insurance or public health systems. There are many variants in the way countries regulate mark-ups, corresponding to differences in policy objectives, including product-oriented approaches (e.g. cost + fixed or regressive percentage), or patient-oriented approaches (e.g. fixed dispensing fees, capitation payments per patient per year).

Patient-oriented approaches delink pharmacy profit and the price or quantity of medicines dispensed, encouraging more rational, efficient, patient-responsive pharmacy practices. In high-income countries (HIC) a combination of the two is often used. Table 1 provides an overview along with potential advantages and disadvantages. (p.15)

Some countries have separate regulation of wholesale and retail mark-ups. Wholesale mark-ups can be limited by setting a maximum allowable mark-up or a maximum price for resale. Some countries ban discounting and rebates by manufacturers and wholesalers to increase transparency of pricing and prevent commercial practices that may contribute to irrational use of medicines.

### How and where has mark-up regulation been implemented?

LMICs most commonly use fixed percentage mark-up regulation. Some control prices either by regulating final retail prices or regulating manufacturer/importer price plus wholesale and retail mark-ups, while others use mark-up regulation alone. WHO/HAI data show some LMICs (India, Iran, South Africa, Syria, Tunisia) apply regressive mark-up regulation (higher priced products incurring lower percentage mark-ups to defined cost thresholds), and Indonesia, Iran, and South Africa use dispensing fees. A few LMICs use selective mark-up regulation for some essential medicines in an attempt to improve affordability. For example, India regulates prices of a small "scheduled" list and Indonesia regulates prices and mark-ups for around 450 unbranded generic medicines, though prices of branded originator and generic products are unregulated. (p.16)

Most OECD countries regulate mark-ups as one component of a comprehensive pricing strategy which also involves setting the manufacturer's or importer's selling price, or profit control or setting the final retail price. Some HICs only regulate prices for reimbursed prescription medicines, while prices and mark-ups for non-reimbursed medicines, over-the-counter medicines and/or hospital medicines are unregulated or subject to different mark-up regulation. Among HICs, all of the options for regulating mark-ups listed in Table 1 can be found, with many variants.



**Table 1. Advantages and disadvantages of mark-up remuneration strategies**

REMUNERATION/MARK-UP (cost price +)	ADVANTAGES / INCENTIVES	LIMITATIONS / DISINCENTIVES
Fixed fee, fees for services	<ul style="list-style-type: none"> <li>No/reduced incentive to sell higher value items</li> <li>Relatively easy to enforce</li> </ul>	<ul style="list-style-type: none"> <li>No incentive to sell lower-cost items</li> <li>Adds significantly to the patient price of low-cost medicines</li> </ul>
Regressive flat fee/amount	<ul style="list-style-type: none"> <li>Reduces incentive to dispense high cost medicines</li> </ul>	<ul style="list-style-type: none"> <li>Reduces incentive to carry high value stock</li> <li>Adds significantly to the patient price of low-cost medicines</li> </ul>
Fixed percentage	<ul style="list-style-type: none"> <li>Relatively simple to implement and enforce</li> </ul>	<ul style="list-style-type: none"> <li>Disincentive to sell lower-cost items</li> <li>Encourage stocking and sale of more expensive items</li> </ul>
Regressive percentage	<ul style="list-style-type: none"> <li>Easy to implement</li> <li>Reduces incentive to dispense high-cost medicines</li> </ul>	<ul style="list-style-type: none"> <li>High-cost items may still attract large value mark-ups</li> <li>May not create incentive to dispense less-expensive items</li> </ul>
Differential percentage or fixed fee	<ul style="list-style-type: none"> <li>Incentives can be created for particular groups of medicines (e.g. essential medicines list, generics)</li> </ul>	<ul style="list-style-type: none"> <li>More complex to implement and enforce</li> </ul>
Fixed maximum fee / percentage	<ul style="list-style-type: none"> <li>Incentive for competition</li> </ul>	<ul style="list-style-type: none"> <li>May lead to reduced service quality or product range in drive to lower costs</li> <li>Disincentive to sell lower-cost items if fixed percentage and inadequate competition or room to reduce costs</li> <li>Incentives exist for retailers to sell more expensive drugs</li> </ul>
Combined mark-up to be divided after negotiation	<ul style="list-style-type: none"> <li>Reduces regulation</li> </ul>	<ul style="list-style-type: none"> <li>Retailers may bypass wholesalers and increase margins/mark-up</li> </ul>
Capitation fees	<ul style="list-style-type: none"> <li>No link to the sale or cost of the medicines</li> <li>No incentive to sell high-cost items</li> </ul>	<ul style="list-style-type: none"> <li>Sophisticated administration systems required</li> </ul>
Capping of mark-ups	<ul style="list-style-type: none"> <li>Reduces incentive to dispense very high-cost items</li> </ul>	
Combinations of above	<ul style="list-style-type: none"> <li>Combinations of above</li> </ul>	<ul style="list-style-type: none"> <li>Combinations of above</li> </ul>

### Key aspects of designing mark-up regulation policies

#### *Consider the incentives and disincentives created*

Fixed percentage mark-ups tend to encourage stocking and sale of higher priced products. Regressive mark-ups are one method to counter this. Patient-oriented approaches seek to separate pharmacists remuneration from the price of the product. Fixed or differential dispensing fees create incentives for dispensing lower-priced products but also create incentives to dispense more items and can disproportionately increase the price of very low-priced products. The benefits of regressive margins or fixed or differential fees can be negated by discounts or other trade schemes which increase the actual profit margin earned by retailers and/or wholesalers. (pp.23-24 and 61-62)

#### *The magnitude and calculation of regulated mark-ups*

What constitutes a reasonable mark-up will differ within and across countries because of differences in geography, level of development, urbanisation, health system structure, procurement price and other factors that affect distribution costs. International comparisons of mark-up levels are not a useful guide. Country-specific cost accounting studies of distribution and pharmacy costs and monitoring of the impact of mark-up regulation can help inform policy. It is important to also consider the effects of mark-up policies on availability, particularly for low-priced medicines, and the viability of pharmacies in remote, sparsely populated areas where distribution costs are high and product

turn-over is low. Low-priced generics may be cheaper than their branded equivalents even with high mark-ups. (pp.45-46)

#### *Complementarity and integration with other policies*

Mark-up regulation needs to be part of a comprehensive regulatory strategy covering manufacturer and importers price, or it is unlikely to control prices effectively. Countries may need to design policies to ensure availability of medicines in remote rural areas where distribution costs are high, such as higher permitted mark-ups, exemption from regulation for low-priced generics, pharmacy subsidies, mobile services, or limited dispensing rights for rural healthcare workers. Promotion of generics and rational use can complement regressive mark-ups and fixed fees. (p.44)

### What capacity and information is required to implement the policy effectively?

Mark-up regulation requires intelligence on costs and profitability in the distribution chain and economic, statistical, medical, pharmaceutical and legal expertise. It requires mechanisms for consulting stakeholders and for monitoring and analysing prices, sales and availability of regulated products, together with resources for enforcement. Studies in a number of LMICs report regulations not being implemented or enforced, and there can be widespread deviations of actual prices from the regulated level in both public and private facilities. [1, 2] (p.47)



### Are there risks associated with mark-up regulation?

If the regulated mark-up is set at an unprofitable level, the availability of regulated medicines may be adversely affected. If most or all medicines are regulated, the commercial viability of some wholesalers or retailers will be reduced, particularly in rural and poor areas with high distribution costs and low product turnover. Fixed percentage mark-ups create incentives for pharmacists to shift stocking and sales to higher priced products and may reduce availability of low-priced generics. Selective regulation of only essential list medicines may lead manufacturers and pharmacists to shift production and sales to more profitable non-essential products. Dispensing fees can add significantly to the prices of low-priced medicines, making them unaffordable for poor patients. Unintended effects can also arise when those in the distribution chain try to recover lost profits.

Regulated companies can be expected to lobby or litigate to overturn the policy, so consultation, involvement of civil society and political support are needed to sustain it. Manufacturers, importers and wholesalers may collude to inflate landed costs. Wholesalers and retailers may introduce additional fees on top of mark-ups. Hospitals may increase other patient fees to make up lost revenue. Unless regulation of mark-ups is part of a comprehensive regulatory process that also covers manufacturers, importers and all agents involved in procurement and distribution, substantial loopholes will exist through which actual mark-ups and medicine prices can be manipulated. Countries can address this by setting a total distribution mark-up or by regulating final patient prices and then using separate regulation or competition or negotiation among firms in the supply chain to determine the actual split between importers, wholesalers, distributors and retailers. (pp.25-27)

### How has the policy been monitored and evaluated?

Monitoring data and evaluation of the regulation of mark-ups in LMICs is sparse and often of poor quality. Countries with better data availability are mostly middle income countries and those with more resources and infrastructure. (pp. 35, 38, 41)

### What effect does the policy have on prices and availability?

Evidence from HICs show that a comprehensive system of price regulation – in which mark-up regulation is one component – can reduce prices and expenditure in the short term [3]. Evidence in LMICs is conflicting and mostly anecdotal. South Africa reported reduced prices of hospital medicines when mark-ups were eliminated [4]. Jordan reported price increases, while Kenya reported price reductions, after removal of price controls [5,6]. Ecuador and Panama perceive that they have more uniform prices

and reduced speculation as a result of mark-up regulation, while Honduras believes it leads to over-invoicing [7]. Use of fixed percentage mark-ups have been found to create incentives for the sale of higher priced medicines in some countries, including China [8]. In China and Mali, selective regulation reportedly has resulted in adverse effects on availability of price-regulated medicines [8,9]. There is no reliable information available about the impact of mark-up regulation alone on medicine prices. No evidence is available on whether regulating discounts and rebates leads to lower prices. (pp.25-27)

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## OTHER USEFUL RESOURCES

A list of useful links and resources, other reviews and policy briefs in this series, and a glossary of terms used in the policy briefs can be found at: [www.haiweb.org/medicineprices/policy/index.html](http://www.haiweb.org/medicineprices/policy/index.html)

## Review 5: Sales Taxes on Medicines

## **Policy brief #5 Pharmaceutical Pricing Policies and Interventions**

WHO/HAI. 2011/2014

WHO/HAI review about taxes on medicines worldwide: a mapping exercise and evidence about impact

97



## SALES TAXES ON MEDICINES

### WHAT IS THE BASIS FOR THIS POLICY BRIEF?

WHO/HAI Review Series on Pharmaceutical Pricing Policies and Interventions. Working paper 5: *Sales taxes on medicines* by Andrew Creese. [www.haiweb.org/medicine-prices/policy/index.html](http://www.haiweb.org/medicine-prices/policy/index.html)



As part of the joint World Health Organization (WHO)/Health Action International (HAI) Project on Medicine Prices and Availability, a series of in-depth reviews have been published on pharmaceutical policies and interventions that may improve medicine availability and affordability. This policy brief summarises the key points from the review on sales taxes and the effects of changes in tax policy on access to medicines, which included a systematic literature review.

*Page references to the review paper are given in parentheses.*

### SUMMARY CONCLUSIONS

#### What is the main case for reducing or eliminating taxes on medicines?

Taxes on medicines can account for a substantial share of medicine prices. They are regressive. They reduce utilisation, particularly by the poor and elderly, and reduce compliance with cost-effective preventive and chronic disease treatment regimes. It makes political, economic and social sense to advocate for a "healthy tax strategy" combining elimination of taxes on some medicines with increases in taxes on unhealthy products and behaviour.

#### What are the main arguments against eliminating medicine taxes?

Taxes are necessary for governments to provide vital public functions and services, including health services.

Medicine taxes can be an important source of revenue. Privileged tax treatment for one sector or type of product can be difficult to defend.

#### Should taxes be reduced or eliminated on all medicine prices?

No. An optimal tax system would treat different medicines differently. A case can be made for cutting taxes on essential medicines – life-saving products, cost-effective chronic disease medicines and medicines with important public health benefits – but not for "lifestyle" medicines and many over-the-counter products.

#### Is the same "healthy tax strategy" appropriate for all countries?

No. Countries differ in the share of revenue lost from cutting medicines taxes and gained from increasing

taxes on various unhealthy products. Constraints on administrative and enforcement capacity in low- and middle-income countries (LMICs) also need to be considered.

#### Are there any complementary policies that should accompany medicine tax reductions?

Price monitoring and analysis is needed to ascertain if tax cuts benefit consumers through corresponding price reductions. Consumers are more likely to benefit if there are complementary policies to stimulate competition where feasible and regulate prices where competition is ineffective.

Taxes commonly make up 20-30% of the final price people pay for medicines (1). Reducing or removing taxes on medicine sales may reduce prices and improve access. The objectives of design of the tax system can be summarised as “to raise money from individuals and the private sector in as efficient, equitable and administratively least costly fashion as possible”. Designing a tax system requires balancing these objectives. The percentage of public revenue raised from medicine taxes appears to be small at 0.03-1.7% of total tax revenue in the sample of country data analysed for the review. (p.21) However, effective tax systems are needed to provide adequate public financing for health services, including financing of medicines to ensure access for the poor. With this in mind, the review looked at whether there is a case for “taxing differently” to improve access to medicines while maintaining or increasing tax revenue. (p. xiii-xiv)

### Direct and indirect taxes in countries with different income levels

Richer countries raise more tax than poor countries as a share of their gross domestic product (GDP). LMICs typically raise a larger share of revenue through *indirect* taxes which are levied on goods and services such as sales taxes and value-added taxes (VAT), compared to richer countries, which raise relatively more *direct* taxes that are levied on the income of individuals and companies. There has been a global trend to replace tariffs on imports and sales taxes with VAT to make the tax system more efficient. Direct taxes can be related to income and so made more or less progressive – meaning that the ‘better off’ pay a larger share of their income in taxes than the poor. But LMICs may have weak capacity to administer income taxes. Indirect taxes are usually regressive – meaning that low-income people pay a larger share of their income in tax than richer people – but can be easier for LMICs to collect. The regressivity of indirect taxes can be reduced by exempting some goods consumed by poorer households from tax or taxing them at a lower rate. (pp.4-7)

### How do different countries tax medicines?

Among 30 European countries with VAT typically with standard rates between 15-25%, five apply a zero VAT rate to some or all medicines. A further 21 countries apply a lower tax rate (ranging from 2.1-11%) to some or all medicines. Where countries apply lower or zero rates only to some medicines, this is usually for prescription medicines or publicly reimbursed medicines, while over-the-counter (OTC) or non-reimbursable medicines are taxed at the standard rate. In the USA, 34 out of 50 states exempt prescription medicines from sales tax or apply a zero rate. Some states also exempt non-prescription medicines. In other states, medicines are commonly exempt from any local government surtaxes on the general state sales tax rate. (pp.9-11)

Medicines taxation in LMICs is less systematically documented. A 2003 study of 57 LMICs found that customs duties accounted for a third of total taxes applied to medicines and found VAT rates on medicines varying from 0% to over 20% (1). The WHO/HAI database (2) on medicine prices shows that in 23 countries where medicines are taxed, the range of tax rates is from approximately 2.9-34%. Ten countries in the dataset report zero VAT or sales tax rates on medicines. The database includes analysis of the component shares of the final retail price accounted for by taxes and other components. Domestic taxes such as VAT or sales tax are the third largest component in the medicines price in many countries after the manufacturer’s selling price and distribution mark-ups. In general, tariffs are a small and falling share of the final price of medicines. Some LMICs have complex taxation arrangements for medicines. India, for example, has two national taxes on most medicines and in addition state governments impose sales taxes. The final impact of tax on retail price is between 13-24%. Medicines sold in the public and private sectors are sometimes taxed differently. Some countries have a variety of additional local charges such as community or local government charges, stamp duty, pharmacy career fees, statistics fees, research fund levies and industrial promotion fund fees. (pp.12-16)

An important difference between high-income countries and LMICs in the impact of medicine taxes on access is the fact that almost all upper income countries have universal or near universal health insurance or public health system coverage, which finances a substantial share of the cost of prescription medicines. In low-income countries, on average around 48% of health spending is out-of-pocket, and the average is several percentage points higher in lower-middle-income countries. Spending on medicines is commonly a high share of out-of-pocket spending. (p.16)



### What effect do reductions in medicines taxes have on prices and availability?

The experience with tax options for medicines and the effects of tax changes on medicines is not well documented. There is a large body of evidence from upper income countries and some from LMICs (3) about the effects of prices for health care, including medicines prices, on demand and utilisation of services, which is relevant. Most of these are studies of user fees and prescription charges rather than tax changes, but in a wide range of circumstances, tax changes should result in corresponding price changes.

An international review of prescription charges concluded that "user charges are a regressive form of health-care finance, requiring the poor to pay more as a proportion of their income than the rich... Poorer people reduced their use of prescription drugs even when co-payment levels were very low" (4). Studies of how much demand for medicines responds to price changes (the "price elasticity of demand") have been carried out in upper-income and LMIC settings. These studies find that medicines, like many other "necessities" have a positive price elasticity less than one – which means that a given percentage increase in price can be expected to result in a smaller percentage reduction in demand or vice versa. Eliminating a 25% tax on

prescription medicines could be expected to increase demand by some 5-15%, if LMIC consumers have comparable price responsiveness to upper income country consumers. Some groups of people, including the poor and the elderly, are more responsive to price changes than others. Responsiveness to price may be lower for medicines for urgent or life-threatening conditions than for some preventive and chronic disease medicines and lifestyle medicines. USA evidence shows that a 10% increase in prescription medicine prices leads to poorer compliance and more frequent discontinuation of treatment, delays in chronically ill patients starting treatment and increased use of health care for chronic conditions (5, 6). (pp. 17-18)

### Complementarity with other policies

Tax changes in some circumstances may not be passed on to consumers fully as corresponding changes in prices. Monopoly suppliers of medicines or cartels may already be charging prices that are as high as the market will bear, and may not be able to increase prices when taxes are imposed without losing revenue, nor face any incentive to cut prices following tax cuts. Policies to increase competition, where feasible, and regulate prices where necessary may be needed in such situations to ensure consumers benefit from any reductions in taxes on medicines.<sup>1</sup> (pp.18-19)

### Removing tax on medicines may not always be effective on its own THE CASE OF PERU

Peru removed indirect taxes on a range of on-patent cancer medicines and anti-retrovirals in 2001, but little change in retail prices was observed as a result. This may indicate that suppliers had monopoly power and faced no incentive to cut prices. Unless complementary policies were to be put in place – for example, an appropriate form of price regulation for on-patent prescription medicines – eliminating taxes would reduce tax revenue without benefiting patients or public funders of health services (7). (pp. 18-19)

### What challenges have been encountered in making the case for medicines tax reductions and how can public health advocates best make the case for tax reductions?

Ministries of Finance tend to oppose tax cuts or exemptions for medicines for several reasons. Governments may stand to lose substantial revenue if medicines taxes are cut. In 57 LMICs studied, VAT revenue on imported medicines alone averaged US\$11.6 million per country, but ranged up to US\$123 million in Brazil and an estimated US\$1 billion in India. Additionally, special cases for tax exemptions for one sector may create precedents for other sectors to lobby for the same privilege. Taxes

on medicines are relatively easy to collect because record-keeping – especially for prescription medicines – is generally better than for many goods. As well, it can be argued that some non-essential medicines are not very different from other commodities in their effect on equity. (pp. 21-22)

A case can be made for tax reductions or exemptions for essential medicines based on the general principles for tax design. Taxes on essential medicines can be shown to be inequitable: the poor and the sick pay a higher share of medicines taxes relative to their income than the rich and healthy. In countries that are unable or unwilling to protect the poor and sick from health care costs through

1. Other policy reviews and policy briefs in this series discuss some forms of price regulation, regulation of mark-ups and competition policy.



public health systems or social health insurance, taxing essential medicines may not only create a barrier to achievement of priority health development goals such as the MDGs for poverty reduction and health, it can also be inefficient. Ill health reduces human capital, reducing their ability to learn, produce and consume. Taxing cost-effective essential medicines thus taxes economic potential. Increased utilisation of medicines for prevention and for management of chronic illnesses can also achieve savings in costs of hospitalization. (pp.23-24)

Public health advocates may be more successful in making the case for cuts in taxes on medicines if they also support the government's efforts to introduce and enforce other forms of tax collection that are more efficient, in particular, taxes on unhealthy products and behaviour, such as excises on tobacco, alcohol and unhealthy foods high in fat, sugar (e.g. taxes on sugary soft drinks) or salt. There may be a stronger case for a "healthy tax strategy" that combines tax cuts with tax increases than for simply cutting medicines taxes. (pp.25-27)

### EXAMPLE The case for a healthier tax strategy in India

In India, the 5% VAT, plus other taxes charged, increases prices and reduces the consumption of essential medicines. Medicine sales in 2009 were reported to be US\$19 billion. VAT revenue alone on medicines would yield almost US\$1 billion. At the same time, tobacco consumption in India reduces life expectancy by an average of 6-10 years. The 38% excise tax on tobacco yields nearly 3% of India's tax revenue, but research has shown that India under-taxes tobacco by not adjusting the excise tax for inflation. Doubling the tobacco excise tax would raise an additional \$3.1 billion in additional revenue each year – enough to allow a complete waiver of VAT on medicines while still allowing a \$2 billion increase in annual government revenue. It would in addition save 3.4 million lives a year (8). (pp.25-26)

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## **Review 4: Competition Policy**

### **Policy brief #4 Pharmaceutical Pricing Policies and Interventions**

WHO/HAI. 2011/2014

WHO/HAI review about competition policies (role of generics) worldwide: a mapping exercise and evidence about impact



# Pharmaceutical Pricing Policies and Interventions

POLICY BRIEF NUMBER 4

106

## COMPETITION POLICY

As part of the joint World Health Organization (WHO)/ Health Action International (HAI) Project on Medicine Prices and Availability, a series of in-depth reviews have been published on pharmaceutical policies and interventions that may improve medicine availability and affordability. This policy brief summarises the key points from the review on competition policy and access to medicines, which included a systematic literature review and a case study of South Africa's use of competition law in medicines markets.

*Page references to the review paper are given in parentheses.*



### WHAT IS THE BASIS FOR THIS POLICY BRIEF?

WHO/HAI Review Series on Pharmaceutical Pricing Policies and Interventions. Working paper 4: *Competition policy* by Loraine Hawkins.  
[www.haiweb.org/medicineprices/policy/index.html](http://www.haiweb.org/medicineprices/policy/index.html)

### SUMMARY CONCLUSIONS

#### Is applying competition law feasible for all LMICs?

No. Competition law is most relevant to middle-income countries with adequate legal systems and state institutions. Low-income country examples of applying competition law to the pharmaceutical sector could not be found.

#### Can competition law be applied to all medicines and all of the pharmaceutical sector?

Yes. Competition law has been applied to every stage of the pharmaceutical supply chain, from product development and manufacturing to dispensing. Competition law does not override the exclusive rights granted to on-patent medicines, but the law is applicable to originator firms if they abuse a dominant position or engage in anti-competitive behaviour to deter generic entry after patent expiry.

#### What are the key pre-requisites for implementing competition law successfully?

- a legal system with adequate competence and independence;
- adequate human and financial resources in the competition authority.

#### Are there any complementary policies needed to support effective price competition?

- credible medicines quality regulation;
- generics policies, including openness to trade in quality assured generics;
- liberal regulation of wholesaling and retail pharmacy to encourage efficient consolidation and reduce distribution costs and improve quality assurance;
- provider payment policies that make health facilities cost-conscious and create incentives for prescribers and dispensers to recommend lowest-priced medicines;

- public support for consumer information and advocacy;
- monitoring systems to identify where competition and regulation are not working.

#### How can competition be promoted in low- and middle-income countries (LMICs) with weak institutions?

In LMICs that cannot implement competition law or medicines quality regulation effectively, market studies to assess competition and regulation can identify a broader range of possible policy interventions that may be more feasible than competition law. Some countries have been able to promote price competition and reduce prices by:

- using the public sector and contracts with NGO or private pharmacies to compete in under-served areas;
- creating supportive conditions for private sector generic pharmacy chains to develop, marketing low-cost generics and providing health advice to low-income clients.



Competition can reduce medicine prices and increase availability if the right conditions are in place. Competition is not effective unless there is credible medicine quality regulation and other supportive policies. Competition law usually has the objective of maintaining and enhancing competition in order to improve consumer welfare. It can help secure competition at all stages of the medicines supply chain. Review of regulations and practices that limit competition may reduce medicines prices. Competition in medicine markets works best when the buyers are price-conscious, expert institutions, such as hospitals, social health insurance agencies, specialist procurement agencies or pharmaceutical benefit management organisations. Institutional buyers can use generic competition to achieve lower prices for off-patent medicines. They can also reduce prices for on-patent products that have close therapeutic substitutes through competition for formulary listing. When individual consumers buy medicines and pay out-of-pocket, competition is imperfect for all but the most familiar over-the-counter medicines. (pp. 5-10)

### What is competition law?

Competition laws usually create powers for a competition authority and the courts to:

1. control mergers and take-overs in order to prevent firms becoming too dominant in a market;
2. prevent anti-competitive agreements among firms, such as price-fixing or sharing out the market among a cartel;
3. prevent dominant firms from abusing their position in the market to the detriment of consumers; and
4. perform market studies to identify where and why competition may be ineffective.

Remedies provided to the authorities to enforce competition law usually include powers to impose fines, to monitor and control prices, to require firms to divest part of a business as a condition of merger, and to require undertakings from companies to cease anti-competitive conduct (1, 3 chapter 3). (pp. 11-12)

### How has competition law been used in medicines markets?

Competition laws have been used to address anti-competitive practices at every stage of the pharmaceutical supply chain. Competition law has been used to penalise originator companies, producers of active pharmaceutical ingredients, generic medicines manufacturers, distributors, retail pharmacies and pharmacy associations that acted to wrongfully inflate prices or restricted availability of medicines. In the USA, the competition authorities have required companies to pay substantial amounts to consumers and state agencies who were harmed by excessive prices. Competition law has been used to prevent merging originator companies from becoming too dominant in particular therapeutic areas.

It has also been used to prohibit them from delaying and deterring generic entry after patents expire. Competition authorities have intervened in mergers between manufacturers and pharmacy benefit management companies to require use of open formularies, selected by independent therapeutics advisory committees. They have required merging

pharmacy chains to divest some branches, to prevent the company becoming too dominant in a locality. They have conducted market studies and reviews of regulation to identify anticompetitive practices that are not in the public interest (2). (pp. 14-17)

### How and where has it been implemented?

Most international experience comes from upper-income countries with high capacity competition authorities and well-functioning courts and law-enforcement. The USA and European Union (EU) have a large body of case law and studies. The experience of some countries that have undergone rapid development in recent decades (such as South Korea, Ireland and the recent EU accession states) may offer lessons for middle-income countries on relevant applications of competition law in the pharmaceutical sector. (p. 4) Since the 1970's there has been increased adoption of competition laws in LMICs, often driven by conditionality in aid programmes, but the pace and effectiveness of implementation has been slow in most of these. There is very limited LMIC experience with applying competition law or conducting market studies in the pharmaceutical sector, with a few exceptions, including Argentina, Brazil, Indonesia, Jordan and South Africa (3, chapters 1 and 3). (p.14)

### What institutional and technical capacity and information is required to implement the policy effectively?

In order to implement competition law effectively, countries need to have:

1. a judicial system with a reasonable degree of independence and competence;
2. functioning third party enforcement of laws, regulations and contracts, free from undue political or industry intervention; and
3. adequate human and financial resources for the competition authority and medicines regulatory agency. (3, chapter 4) (p. 41)



### Complementarity with other policies

A range of other policies are important for promoting competition to reduce prices, while assuring the quality and availability of medicines. Most of these policies can also be effective in countries without functioning competition laws. Key policies that can support effective competition, if they are well designed and implemented, include the following:

- *increasing the credibility, efficiency and transparency of the national medicines regulatory agency*: Without credible regulation, prescribers and patients will prefer higher-priced originator products and premium-branded generics and may perceive lower prices as an indicator of lower quality. (p. 24)
- *generics policies*: Competition can be promoted by flexible provisions in intellectual property and pharmaceutical laws permitted under TRIPS to expedite entry of generics into the market after patent expiry, and by permitting imports of quality-assured generics with zero tariffs. Mandating or promoting generic prescribing or permitting generic substitution by pharmacists can also stimulate generic competition, but is only likely to be effective if medicine quality regulation is credible, and needs to be supported by doctor and pharmacist education and financial incentives. (pp. 20, 25-26)
- *competitive public procurement*: National and regional procurement agencies may be able to achieve lower procurement prices than smaller local health authorities or facilities. (p. 19)
- *using the public sector and contracts with NGO or private pharmacies or accredited drug stores to increase competition while assuring quality*: In LMICs such as Kyrgyzstan and Tanzania, this has been effective in areas where the poor are under-served, such as remote rural areas and urban slums. Some countries (e.g. New Zealand, Brazil) have successfully reduced prices by distributing publicly procured generic medicines through private pharmacies (4,5). (p. 23)
- *provider payment and medicine reimbursement policies that create incentives for competition in the supply chain*: Health insurance agencies or public health systems can include medicines costs in the prices they pay for healthcare services (e.g. in global budgets or case-based payments for hospitals), to encourage providers to dispense low-cost generics. They can use competition for formulary listing and for setting reimbursement rates. They can design remuneration systems for private community pharmacists to give them incentives to dispense low-cost generics (6,7). (pp. 21-23)
- *consumer information and protection policies*. This can encompass regulation of advertising and promotion, professional ethical codes to protect consumers from misinformation, education campaigns and advocacy to promote generic medicines as "good value". (p. 24)

- *removal of regulatory barriers to efficient distribution and retail pharmacy*: overly restrictive regulations of over-the-counter sales of medicines, of retail pharmacy ownership and location, of the pharmacy profession and of wholesale distribution can restrict competition and prevent efficient consolidation of medicines distribution. Countries that allow efficient combination of integration and competition appear to be best placed to achieve lower mark-ups on sales of medicines. Pharmacy chains with their own distribution system can help to build consumer confidence in the quality of generic medicines sold (8). (pp. 26-30)

### PRIVATE SECTOR COMPETITION FROM GENERIC PHARMACY CHAINS

Emergence of new private pharmacy chains marketing low-cost generics to lower-income customers has occurred in Mexico (*Farmacia Similares*) and the Philippines (*The Generics Drugstore*). These chains brought price competition into areas that had previously been served by a mix of high-priced market-dominant chains and inefficient independent drug stores and spread into rural market towns, improving rural access. Private sector competition was fostered by:

- liberal pharmacy regulation permitting chains, corporate, distributor-retail integration;
- a franchise model that enabled rapid growth, mobilised capital from small investors;
- public promotion of generics by advocacy for generics medicine legislation.

### What effect does the policy have on prices and availability?

There is extensive good quality evidence from upper income countries and some evidence from LMICs that competition can reduce prices for essential medicines in retail pharmacies. Much of this comes from studies of the price reductions and market share changes after generic competitors enter the market. Some comes from studies of internal reference price schemes. Studies of competitive tendering and of competition for formulary listing demonstrate price reductions achieved by institutional purchasers. (pp. 5-6) Economic evaluations of the impact of competition law do not provide findings specifically about the pharmaceuticals sector. However, analyses, case reports and settlement agreements of competition authorities such as the Federal Trade Commission in the USA and the Competition Commission in South Africa document evidence of price and other effects of anti-competitive behaviour and competition law rulings. (3, 8) Although low-income country evidence is sparse, a study of the effects of retail pharmacy competition in rural Kyrgyzstan found that a new pharmacy could bring about price reductions in districts up to 15 kilometres away (4).



### What are the challenges and risks associated with the policy in LMICs?

Unclear law, technically weak decision-making and variable enforcement are challenges in a number of LMICs that can lead to inconsistent and unpredictable application of the law, with unintended negative effects, including the risk of deterring entry of new, more efficient businesses or deterring efficient consolidation of fragmented sectors like the pharmaceutical sector. In countries with weak capacity in

competition authorities and the courts, the processes involved in competition law deliberations and enforcement can be too slow and costly. At worst, in countries with weak legal systems, where powerful, concentrated business interests are combined with a lack of political will to confront those interests, competition law may be evaded by those with connections and enrich corrupt officials and politicians (3, chapters 6, 7 and 9). (pp. 15-16)

#### COUNTRY CASE STUDY: SOUTH AFRICA (pp. 31-39)

South Africa adopted a new Competition Act in 1998 after an inclusive policy process. The Competition Commission has since considered a range of cases covering:

- abuse of dominant market position by multinational manufacturers;
  - exclusive distribution agreements used by multinationals;
  - mergers of retail pharmacy chains;
  - collusion in public procurement by local firms.
- Substantial fines, orders to divest, and undertakings to change conduct have been imposed under the new law.

#### What specific challenges were encountered and what lessons can be learned?

As a new agency with limited resources, the Competition Commission increased its impact by choosing strategically important cases to set precedents, and used public education and guidance to encourage the whole sector to comply with the principles established by landmark cases. Its willingness to tackle a high profile case concerning in-patent antiretroviral medicines of high public health importance was important for credibility. The Commission and consumer groups mobilised international technical and donor resources to build specialist capacity and support legal action.

#### How has the policy been monitored and evaluated?

South Africa established a committee to monitor prices and recommend actions needed from the Competition Commission, the health and medicines authorities or other agencies. This reflects a judgement that competition law – though beneficial – is not enough on its own to protect consumers from paying higher prices for medicines than they need to (9, 10).

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# Pharmaceutical policies: effects of reference pricing, other pricing, and purchasing policies

Aaserud M, Dahlgren A, Kosters J, Oxman A, Ramsay C, Sturm H. 2006  
Report for Cochrane Database of Systematic Reviews

110

## ABSTRACT

### Background

Pharmaceuticals can be important for people's health. At the same time drugs are major components of health care costs. Pharmaceutical pricing and purchasing policies are used to determine or affect the prices that are paid for drugs. Examples are price controls, maximum prices, price negotiations, reference pricing, index pricing and volume-based pricing policies. The essence of reference pricing is to establish a maximum level of reimbursement for a group of drugs assumed to be therapeutically equivalent.

### Objectives

To determine the effects of pharmaceutical pricing and purchasing policies on drug use, healthcare utilisation, health outcomes and costs (expenditures).

### Search strategy

We searched the following databases and web sites: Effective Practice and Organisation of Care Group Register (date of last search: 22/08/03), Cochrane Central Register of Controlled Trials (15/10/03), MEDLINE (07/09/05), EMBASE (07/09/05), ISI Web of Science (08/09/05), CSA Worldwide Political Science Abstracts (21/10/03), EconLit (23/10/03), SIGLE (12/11/03), INRUD (21/11/03), PAIS International (23/03/04), International Political Science Abstracts (09/01/04), NHS EED (20/02/04), PubMed (25/02/04), NTIS (03/03/04), IPA (22/04/04), OECD Publications & Documents (30/08/05), Source OECD (30/08/05), World Bank Documents & Reports (30/08/05), World Bank e-Library (04/05/05), JOLIS (22/08/05), Global Jolis (22/08/05 and 23/08/05), WHOLIS (29/08/05).

### Selection criteria

Policies in this review were defined as laws, rules, financial and administrative orders made by governments, non-government organisations or private insurers. To be included a study had to include an objective measure of at least one of the following outcomes: drug use, healthcare utilisation, health outcomes, and costs (expenditures); the study must be a randomised controlled trial, non-randomised controlled trial, interrupted time series analysis, repeated measures study or controlled before-after study of a pharmaceutical pricing or purchasing policy for a large jurisdiction or system of care.



**Data collection and analysis**

Two reviewers independently extracted data and assessed study limitations. Quantitative analysis of time series data, for studies with sufficient data, and qualitative analyses were undertaken.

**Main results**

We included 10 studies of reference pricing and one study of index pricing. Most of the reference pricing studies were for senior citizens in British Columbia, Canada. The use (dispensing) of reference drugs increased in five studies, between 60% and 196% immediately after introduction of reference drug pricing, whereas the use of cost sharing drugs decreased by between 19% and 42% in four studies. In three studies the reference drug group expenditures decreased (range 19% – 50%), whereas in the fourth study the expenditures increased by 5% in the short term. The results after six months of reference pricing do not show any clear pattern in relationship to the immediate effects. We found no evidence of adverse effects on health and no clear evidence of increased health care utilisation. For index pricing the evidence was much more limited than for reference drug pricing. A small reduction in drug prices was found.

**Authors' conclusions**

We found relatively few studies of pricing policies. The majority of the studies dealt with reference pricing. They had few methodological limitations. Based on the evidence in this review, mostly from senior citizens in British Columbia, Canada, reference drug pricing can reduce third party drug expenditures by inducing a shift in drug use towards less expensive drugs. We found no evidence of adverse effects on health and no clear evidence of increased health care utilisation. The analysis and reporting of the effects on patient drug expenditures were limited in the included studies and administration costs were not reported.

# Measuring medicine prices, availability, affordability and price components

WHO and Health Action International. 2008  
Second edition of manual for price survey

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# 1

## Introduction

### 1.1 WHY MEASURE THE PRICE AND AVAILABILITY OF MEDICINES?

One third of the global population lacks reliable access to needed medicines (1). The situation is even worse in the poorest countries of Africa and Asia, where as much as 50% of the population lacks such access. While some 10 million lives a year could be saved by improving access to essential medicines and vaccines – 4 million in Africa and South-East Asia alone (2) – a major obstacle to achieving this has been price.

Average per capita spending on pharmaceuticals in high-income countries is 100 times higher than in low-income countries – about US\$ 400 compared with US\$ 4. The World Health Organization (WHO) estimates that 15% of the world's population consumes over 90% of the global production of pharmaceuticals (by value) (3).

Access to health care is a fundamental human right, enshrined in international treaties and recognized by governments throughout the world. However, without equitable access to essential medicines for priority diseases the fundamental right to health cannot be fulfilled. Access to essential medicines is also one of the United Nations' Millennium Development Goals (MDGs) (1).

In developing countries today medicines account for 25–70% of overall health-care expenditure, compared to less than 10% in most high-income countries (1,3). The cost of newer products with proven advantage over older medicines, such as antiretrovirals, medicines for tuberculosis and new antimalarials, limits access to medicines in resource-poor settings. Moreover, up to 90% of the population in low- and middle-income countries must pay for medicines out of pocket due to lack of social insurance and inadequate publicly subsidized services (1,4). Not only are medicines unaffordable for large sectors of the global population, they are a major burden on government budgets.

In Member Countries of the Organization for Economic Co-operation and Development (OECD), many direct and indirect pharmaceutical price regulations remain in effect (5,6). However, in many low- and middle-income countries, national medicine pricing policies have been shifting from price controls to deregulation under the influence of structural adjustment and reform programmes.

Duties, taxes, mark-ups, distribution costs and dispensing fees are often high, regularly constituting between 30 to 45% of retail prices, but occasionally up to 80% or more of the total (7-9). The higher the manufacturer's selling price, the more these elements increase the final price. Prices are also influenced by factors



such as whether the country observes patents and the level of flexibility allowed under international treaties – which is eventually incorporated into national patent law; the level of domestic medicine production; national policies on protecting local industries; the level of competition between pharmaceutical manufacturers; and price regulation policies.

National policies, medicine pricing and procurement strategies are required to ensure that medicines are affordable (1). While policies are also greatly needed to improve health infrastructure and financing as well as to ensure the rational use of medicines, high medicine prices are one of the biggest obstacles to access. Nevertheless, even in the face of a weak infrastructure and poverty, improvements in access can be achieved (10).

The difficulty in finding reliable information on medicine prices and availability – and therefore in analysing their components – hinders governments in constructing sound medicine pricing policies or evaluating their impact. It also makes it difficult for them to evaluate whether their expenditure on medicines is comparable to that of other countries at a similar stage of development. Moreover, those responsible for purchasing medicines cannot negotiate cheaper deals because they have no sound basis from which to start their negotiation. Even in countries where consumers and patients have greater purchasing power, governments, insurance funds and hospitals often find it difficult to decide on the selection of medicines because they lack information.

Prices of the same medicines frequently vary between countries (11); some commonly used medicines have been found to be more expensive in developing countries than in industrialized ones (12-14); and many studies have shown that affordability is unrelated to purchasing power. The ex-manufacturer prices to countries – in particular for the private sector – are often confidential. Medicine price indicator guides<sup>1</sup> provide the sales prices from large wholesalers of generically equivalent medicines to governments. However, they do not give the price patients must pay in either the public or private sectors and often do not include new, essential but patented medicines. A few countries have publicly available prices, but the information's use is obstructed by the country-specifics that apply and language barriers. The monitoring of prices and cross-country comparisons are therefore important.

## **1.2 THE WHO/HAI PROJECT ON MEDICINE PRICES AND AVAILABILITY**

### **1.2.1 Background and project objectives**

In the mid-1990s, civil society organizations in developed and developing countries – including Health Action International (HAI), Médecins Sans Frontières (MSF), the Consumer Project on Technology and Oxfam – started drawing attention to the need for increased access to medicines as part of the fight against poverty. Unaffordable medicine prices were considered a barrier to accessing treatment, but at this time only a few small-scale studies in developing countries had been carried out to measure medicine prices and make international comparisons. Methodological difficulties left many of these studies' results open to criticism.

Study results by HAI Asia Pacific (13,14) and others were discussed with WHO at the WHO/Public Interest NGO Roundtables held in the late 1990s. While it appeared that prices were higher in low-income countries compared to some more

<sup>1</sup> Management Sciences for Health (MSH); the WHO Regional Office for Africa; UNICEF/UNAIDS/WHO-HTP/MSF.



wealthy nations, relatively little was known about prices in different settings in low- and middle-income countries, and about the factors that make up the final patient price. The absence of a standard methodology was seen as a stumbling block in reliable price measurement and international comparison.

Both WHO and the nongovernmental organizations (NGOs) recognized that the availability and affordability of essential medicines had to be improved through developing evidence-based national policies and programmes. To this end, the WHO/HAI Project on Medicine Prices and Availability was established in 2001 to:

- develop a reliable methodology for collecting and analysing medicine price, availability, affordability and medicine price component data across health-care sectors and regions in a country;
- publish survey data on a publicly accessible web site to improve price transparency; and
- advocate for appropriate national policies and monitor their impact.

In May 2001, delegates to the World Health Assembly endorsed and gave further support to the project. They requested WHO “to explore the feasibility and effectiveness of implementing, in collaboration with NGOs and other concerned partners, systems for voluntary monitoring [of] drug prices and reporting global drug prices with a view to improving equity in access to essential drugs” (15). A year later, the World Health Assembly called on WHO to “provide technical support, especially to developing countries, to establish drug-pricing policies” (16).

### 1.2.2 Development, testing and use of the manual

In Phase I of the project, WHO, HAI and a group of international experts drafted a methodology to measure medicine prices, availability, affordability and price components. Following pilot testing in Armenia, Brazil, Cameroon, Ghana, Kenya, Peru, the Philippines, South Africa and Sri Lanka, the methodology was launched at the 2003 World Health Assembly as a draft manual and Excel workbook for field testing (17). Despite considerable pilot testing, HAI and WHO viewed the first edition of the manual and workbook merely as a starting point. As more surveys were undertaken, the methodology was kept under review and further developed in collaboration with survey managers in the light of accumulating experience.

To improve price transparency, a database of survey results was established on HAI’s web site.<sup>1</sup> This enables international comparisons to be made, since all surveys have used the WHO/HAI standardized approach. In addition to the database, the web site also provides all survey documents, any updates to the methodology, survey reports, advocacy material as well as project and related publications.

In Phase II of the project (which began mid-2003), HAI, WHO and project members provided technical assistance to ministries of health, NGOs, university researchers and others who undertook national or provincial/state surveys using the WHO/HAI methodology. This assistance was provided through regional pre- and post-survey workshops (in anglophone and francophone Africa, Asia/Pacific, Central Asia, the Eastern Mediterranean and India), various national workshops and through online advice.

During Phase II, studies were undertaken to validate the sampling methodology, the volatility of the reference prices and to compare actual prices paid with those

<sup>1</sup> [www.haiweb.org/medicineprices](http://www.haiweb.org/medicineprices)



collected by data collectors. The results confirmed the strength and appropriateness of the WHO/HAI approach.

At the request of survey managers, a system to regularly monitor medicine prices, availability and affordability was developed and piloted in various countries in Africa and Asia in Phase II of the project (see Chapter 14).

### 1.2.3 Survey results

By the end of 2007, over 50 surveys had been undertaken across the globe, from Cameroon and the Cook Islands to El Salvador, South Africa and the Syrian Arab Republic. They have generated reliable evidence showing, for the first time, some startling facts about the affordability and availability of medicines. The results of these surveys<sup>1</sup> revealed that in many low- and middle-income countries:

- medicine prices are high, especially in the private sector (e.g. over 80 times an international reference price);
- availability can be low, particularly in the public sector (including no stocks of essential medicines);
- treatments are often unaffordable (e.g. requiring over 15 days' wages to purchase 30 days' treatment);
- government procurement can be inefficient (e.g. buying expensive originator brands as well as cheaper generics);
- mark-ups in the distribution chain can be excessive; and
- numerous taxes and duties are being applied to medicines.

The results confirm that in many countries access to essential medicines is hindered by low availability and unaffordable prices. For example, salbutamol inhaler – an important medicine used to treat asthma – is virtually unavailable in the public sector of many countries (where medicines are generally cheaper or even free) and when purchased from the private sector, can cost the lowest-paid, unskilled government worker several days' wages (Table 1.1). As Fig. 1.1 illustrates, people are paying high prices for many medicines. The price of originator brand atenolol 50 mg tablets is over 20 times the international reference price in all the countries except India (where it is still high at 5 times the reference price) and Kazakhstan. Even the lowest-priced generic is very expensive in all countries, and there are some huge brand premiums, e.g. in Uganda the originator brand is about 13 times the price of the generic.

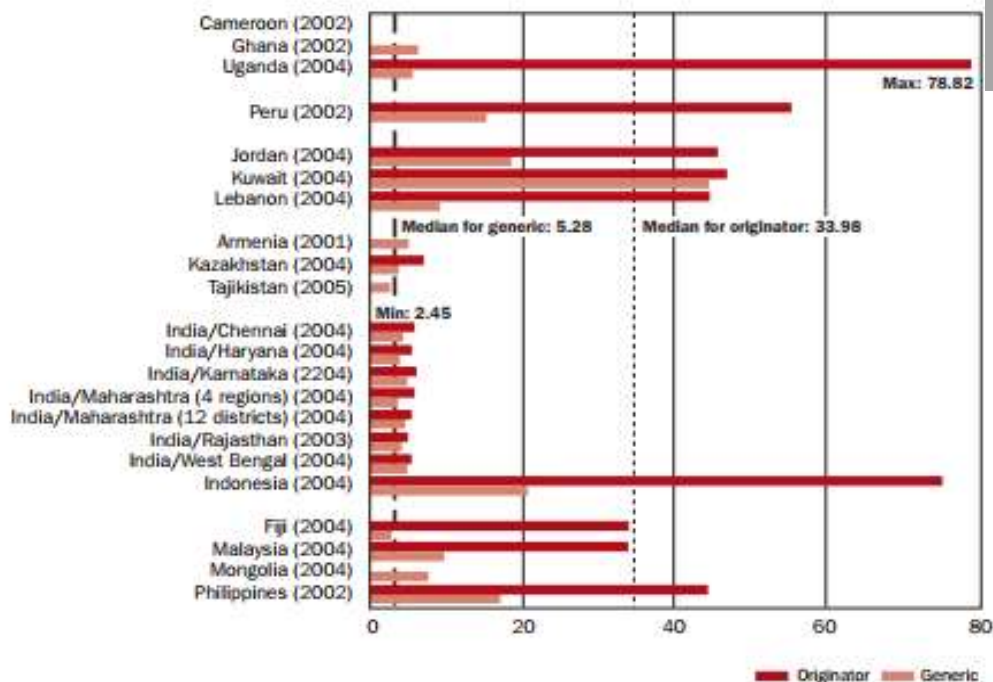
**Table 1.1 Availability and affordability of 1 salbutamol inhaler 0.1mg/dose in selected countries<sup>a</sup>**

	Availability - public sector facilities		Affordability - private sector facilities	
	Originator	Lowest-priced generic	Originator	Lowest-priced generic
Uganda, April 2004	0%	0%	5.6 days	2.0 days
Ghana, October 2004	4%	11%	8.0 days	4.6 days
Mali, March 2004	0%	0%	4.2 days	2.7 days
Pakistan, July 2004	0%	3%	1.4 days	1.4 days
Indonesia, August 2004	13%	0%	4.1 days	-

<sup>a</sup> Results of national medicine price and availability surveys conducted using WHO/HAI standard methodology. Data are available from <http://www.haiweb.org/medicineprices/>.

<sup>1</sup> <http://www.haiweb.org/medicineprices>

Fig. 1.1 Median price ratios, atenolol 50 mg tablets, purchased from private retail pharmacies



Source: Gelders S et al. Price, availability and affordability: an international comparison of chronic disease medicines. Cairo, World Health Organization, 2006.

Regional analyses of data have been undertaken or are currently being drafted for surveys conducted in India (18), the WHO Eastern Mediterranean Region (19) and the WHO African Region (20), respectively, as well as Central Asia. An international comparison of prices, availability and affordability of medicines to treat chronic diseases has also been done (21), and analyses of price and availability of medicines in various therapeutic groups are underway. Reports of these analyses can be found on the HAI web site.

#### 1.2.4 Evidence for policy development and implementation

The project's objective is to improve the availability and affordability of essential medicines through the development of evidence-based national policies and programmes. It has been encouraging, therefore, to see survey reports being disseminated and findings discussed in different national, regional and global forums.

Following the 2006 World Health Assembly, the *British Medical Journal* published an editorial drawing attention to the WHO/HAI report on prices, availability and affordability of chronic disease medicines that stated "the report's findings make explicit what has long been recognized: that the cost of medical care impoverishes or is simply beyond the reach of many people in developing countries. Amid the gloom, however, there is some light. Simply collecting data and presenting it to governments can stimulate action" (22). Indeed, some countries have acted on the evidence, among them the Government of Indonesia, which reduced the price of 458 generic medicine formulations from 5%–70% and implemented regulations to standardize prices for all public purchasing; the Government of Lebanon, which reduced the prices of a quarter of medicines on the market and introduced regressive



mark-ups; the Government of Nigeria, which is drafting a medicines policy, based on its survey findings; and the Government of Tajikistan, which abolished 20% VAT on medicines. In Phase III, the project will support countries to develop and implement policies and programmes that result in improved availability of medicines and more affordable treatments. Additionally, the project will support establishing national monitoring systems to evaluate the impact of policy changes (see Chapter 14).

Changes in national policies feature in the project's bulletin *Medicine Pricing Matters* along with publications and other interesting outcomes of pricing work being carried out worldwide. This quarterly bulletin was first published in December 2007.<sup>1</sup>

### 1.2.5 Related surveys and initiatives

It has been encouraging to see other price studies utilizing the WHO/HAI survey methodology. In Nepal and Nicaragua, John Snow International and PATH conducted a survey of commodities for reproductive health (OCP, IUD, condoms, vaccines and other medicines) using an adaptation of the WHO/HAI methodology (23, 24). In 2005, WHO's Noncommunicable Diseases and Mental Health Cluster used the WHO/HAI methodology to survey the price, availability and affordability of 35 medicines used to treat chronic conditions (25). The surveys were done in Bangladesh, Brazil, Malawi, Nepal, Pakistan and Sri Lanka. More recently, the Medicines for Malaria Venture (MMV) has conducted a survey in Uganda looking at the price, availability, affordability and quality of all antimalarials on the market, using and adaptation of the WHO/HAI methodology.<sup>2</sup> MMV is planning to conduct a number of surveys in other countries.

The Medicines Transparency Alliance (MeTA) is a new initiative of the United Kingdom Department for International Development (DFID). MeTA will work with national and international partners, including WHO and the World Bank, to support national efforts to enhance transparency and build capacity in medicines policy, procurement and supply chain management. DFID envisages international actors supporting national efforts, coupled with focused technical and financial support to strengthen transparency and accountability. Such national efforts would seek to improve access to information about medicine quality, availability and pricing, with strong civil society and consumer involvement in scrutiny and debate. MeTA has identified the WHO/HAI price measurement methodology as the key tool for measuring medicine prices, availability, affordability and component costs. MeTA will be launched in May 2008, with pilots in several countries in Africa, Asia, Central Asia, the Eastern Mediterranean and Latin America.<sup>3</sup>

## 1.3 THE MEDICINE PRICES AND AVAILABILITY SURVEY MANUAL – SECOND EDITION

Published in 2003, the first WHO/HAI medicine prices manual *Medicine Prices – A New Approach to Measurement. Draft for field-testing* provides a draft methodology and tools to conduct national medicine prices and availability surveys. This second

<sup>1</sup> Contact HAI if you wish to be placed on the mailing list. WHO's *Essential Drugs Monitor* (<http://www.who.int/medicines/publications/monitor/en/index.html>) regularly features articles on medicine pricing work and the 33rd issue (<http://mednet2.who.int/edmonitor/33/mon33.html>) carried a 16-page supplement on survey findings and analyses, policy changes and advocacy. Contact [edmdoccentre@who.int](mailto:edmdoccentre@who.int) to receive a copy of this edition or to be placed on the mailing list.

<sup>2</sup> [http://www.mmv.org/IMG/pdf/Prices\\_of\\_Antimalarials\\_MMV\\_survey\\_July\\_07\\_website\\_19\\_Sept.pdf](http://www.mmv.org/IMG/pdf/Prices_of_Antimalarials_MMV_survey_July_07_website_19_Sept.pdf)

<sup>3</sup> Additional information on MeTA can be found at <http://www.dfidhealthrc.org/MeTA/index.html>



edition of the survey manual has been updated to reflect the wealth of practical experience in conducting medicine prices and availability surveys garnered in the project's first two phases.

The new manual and accompanying tools have been developed through a consultative process with project participants, national collaborators and the WHO/HAI Project on Medicine Prices Steering and Advisory Groups. A technical meeting was held in Cairo from 27 November to 3 December 2006 with the medicine prices project management team, advisory and steering groups, selected survey managers and consultants to recommend changes to the methodology and revisions to the survey manual. This group has also been consulted throughout the manual revision process, and has contributed to sections of the manual related to their respective areas of expertise.

In the manual's second edition, the survey methodology has been refined, based on the lessons learnt in the more than 50 surveys conducted to date. New methodologies and tools have also been developed in the areas of price component surveys (Chapter 9) and routine monitoring of medicine prices and availability (Chapter 14). The revised manual also provides significantly more guidance in the areas of policy options and lines of action (Chapter 11) as well as advocacy strategies aimed at stimulating reform of medicine price policies (Chapter 13).

The second edition includes the revised survey manual along with updated versions of the automated data workbooks and survey instruments: it also includes a CD-ROM of survey tools, resources and background materials. The CD-ROM and the HAI web site<sup>1</sup> will be updated periodically with new materials as these become available.

Feedback on the second edition of the medicine prices and availability survey manual is welcome and encouraged.<sup>2</sup>

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<sup>1</sup> <http://www.haiweb.org/medicineprices/>

<sup>2</sup> Please contact HAI ([info@haiweb.org](mailto:info@haiweb.org)) or WHO ([medicineprices@who.int](mailto:medicineprices@who.int)).



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## Determinants of branded prescription medicine prices in OECD countries

Kanavos PG, Vondoros S. 2011

Article published in Health Economics Policy and Law; investigation of determinants of the prices of branded prescription medicines in 15 OECD countries

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### Determinants of branded prescription medicine prices in OECD countries.

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#### Abstract

This paper investigates the determinants of the prices of branded prescription medicines across different regulatory settings and health care systems, taking into account their launch date, patent status, market dynamics and the regulatory context in which they diffuse. By using volume-weighted price indices, this paper analyzes price levels for a basket of prescription medicines and their differences in 15 OECD countries, including the United States and key European countries, the impact of distribution margins and generic entry on public prices and to what extent innovation, by means of introducing newer classes of medicines, contributes to price formation across countries. In doing so, the paper seeks to understand the factors that contribute to the existing differences in prices across countries, whether at an ex-factory or a retail level. The evidence shows that retail prices for branded prescription medicines in the United States are higher than those in key European and other OECD countries, but not as high as widely thought. Large differences in prices are mainly observed at an ex-factory level, but these are not the prices that consumers and payers pay. Cross-country differences in retail prices are actually not as high as expected and, when controlling for exchange rates, these differences can be even smaller. Product age has a significant effect on prices in all settings after having controlled for other factors. Price convergence is observed across countries for newer prescription medicines compared with older medicines. There is no evidence that originator brand prices fall after generic entry in the United States, a phenomenon known as the 'generics paradox'. Finally, distribution and taxes are important determinants of retail prices in several of the study countries. To the extent that remuneration of the distribution chain and taxation are directly and proportionately linked to product prices this is likely to persist over time.

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## Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis

Cameron A, Ewen M, Ross-Degnan D, Ball D, Laing R. 2009  
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### Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis.

Cameron A<sup>1</sup>, Ewen M, Ross-Degnan D, Ball D, Laing R.

[+ Author information](#)

#### Erratum in

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#### Abstract

**BACKGROUND:** WHO and Health Action International (HAI) have developed a standardised method for surveying medicine prices, availability, affordability, and price components in low-income and middle-income countries. Here, we present a secondary analysis of medicine availability in 45 national and subnational surveys done using the WHO/HAI methodology.

**METHODS:** Data from 45 WHO/HAI surveys in 36 countries were adjusted for inflation or deflation and purchasing power parity. International reference prices from open international procurements for generic products were used as comparators. Results are presented for 15 medicines included in at least 80% of surveys and four individual medicines.

**FINDINGS:** Average public sector availability of generic medicines ranged from 29.4% to 54.4% across WHO regions. Median government procurement prices for 15 generic medicines were 1.11 times corresponding international reference prices, although purchasing efficiency ranged from 0.09 to 5.37 times international reference prices. Low procurement prices did not always translate into low patient prices. Private sector patients paid 9-25 times international reference prices for lowest-priced generic products and over 20 times international reference prices for originator products across WHO regions. Treatments for acute and chronic illness were largely unaffordable in many countries. In the private sector, wholesale mark-ups ranged from 2% to 380%, whereas retail mark-ups ranged from 10% to 552%. In countries where value added tax was applied to medicines, the amount charged varied from 4% to 15%.

**INTERPRETATION:** Overall, public and private sector prices for originator and generic medicines were substantially higher than would be expected if purchasing and distribution were efficient and mark-ups were reasonable. Policy options such as promoting generic medicines and alternative financing mechanisms are needed to increase availability, reduce prices, and improve affordability.

#### Comment in

[Better measures of affordability required.](#) [[Lancet](#). 2009]

[Essential medicines pricing--reform needed.](#) [[Lancet](#). 2009]

PMID: 19042012 DOI: [10.1016/S0140-6736\(08\)61762-6](#)

## Executive summary

**N**ew technologies are entering health care systems at an unprecedented pace: remote sensors, robotics, genomics, stem cells, and artificial intelligence are on the cusp of becoming a normal part of medical care. Medicines can now be combined with nanotechnologies and digital tools. 3D printing is already used to manufacture implants, and bioprinting is expected soon to modify organ transplantation. Precision medicine, which establishes links between individuals' biology and their diseases, promises to increase our understanding of diseases and help better target treatments. Vast amounts of electronic data related to health and wellness are being generated by health systems and by individuals. Collectively, these data hold valuable information that could foster improvement in all health system activities, from clinical care to population health, to research and development.

These new technologies provide immense opportunities but also raise novel challenges for all health stakeholders, including policy makers, regulatory authorities, payers, physicians and patients.

New technologies challenge regulatory pathways in many ways. New types of products often combine technologies (medical devices, diagnostics and medicines) that are typically assessed before market entry by separate entities. The development of precision medicine, especially in cancer, involves new forms of clinical trials, sometimes including very few patients, questioning current standards for market approval. Regulators are pressured to provide rapid access to medicines for severe conditions with no available alternative.

Regulators recognise the need to strengthen regulation of medical devices, which has traditionally been less stringent than that of pharmaceuticals. The burgeoning field of mobile health (mHealth) is also a challenge for policy makers. The sheer volume and variety of new mHealth products, as well as the risks related to security of personal health data, calls for new regulatory models to determine what is safe and useful to patients, providers and the public.

More needs to be done after market entry to ensure sustainable access to innovative therapies while guaranteeing safety and efficient use of resources. Too often, products are only assessed for safety and performance at market entry. Monitoring these aspects as well as clinical utility in real life can manage risks for patients and identify devices that perform better than others.

In the pharmaceutical sector, the proliferation of high-cost medicines calls current pricing models into question. The launch prices of drugs for cancer and rare diseases are increasing, sometimes without commensurate increase in health benefits for patients. Payers increasingly struggle to pay for high-cost medicines targeting very small populations, which are becoming the "new normal" in the pharmaceutical sector. New treatments for



hepatitis C, which are very effective and cost-effective, are unaffordable to many who would benefit in almost all OECD countries because of their high budget impact.

Despite much discussion about the potential of Big Data and information systems for public health goals of research, health system improvement and disease surveillance, progress is needed in many countries to set laws and policies that permit and enable use of health and health care data in a secure fashion.

Technology can only generate value in health care systems if the health benefits of these technologies outweigh the costs they impart. This can only be achieved by promoting access to and appropriate use of technologies that are safe, performant, effective and clinically useful.

This report analyses policies affecting the use of pharmaceuticals, medical devices, precision medicine, and digital technology (mainly the use of health data). It recommends policy makers to:

### **Steer investments in biomedical research and development (R&D) and prepare for upcoming technologies in the health sector**

- Further co-ordinate efforts to identify gaps in global biomedical R&D and encourage research through co-operation between countries and stakeholders, with well-designed incentives.
- Engage in co-operative horizon scanning to better prepare for new technologies that have the potential to be disruptive or to raise financing challenges.

### **Adapt policies to regulate market entry of new technologies**

- Ensure that quicker access to promising pharmaceuticals for severe unmet needs does not unduly compromise patient safety. Patients should be adequately informed about the quasi-experimental status of products with incomplete pre-market evidence.
- Strengthen regulation of medical devices to improve safety and performance, especially for those associated with higher patient risk. Improve post-market surveillance, notably through the implementation of a system that enables product identification. Increase efforts to monitor performance of medical devices in routine clinical use by leveraging health data, and share information across countries and regions.
- Adapt regulation to new technology types, including hybrid technologies, by promoting co-ordination between entities that typically manage separately different types of technologies.
- Adopt a regulatory framework for mHealth products, which ensures safety and manages risks to privacy and security, encourages high-value innovation, and prevents ineffective, unsafe and low-value products from flooding the market and crowding out the more beneficial ones.

### **Use health technology assessment, coverage and pricing policies to encourage value-for-money**

- Use new methods to guarantee quicker access to treatments where effectiveness is uncertain or very different across indications, while also seeking to reduce uncertainty about the impact of treatments. Coverage with evidence development schemes, that have been used for pharmaceuticals (e.g. in the Netherlands, Sweden, and the United States) or

for medical devices (e.g. in Australia, France, Germany, the Netherlands, Switzerland, the United Kingdom and the United States), can be used, provided that new evidence is produced on time and coverage conditions are revised accordingly.

- Promote a “ifecycle approach” for Health Technology Assessment (HTA) across all types of biomedical technology, whereby coverage and pricing decisions are not set only once at market entry, but regularly re-assessed.
- Develop methods to produce evidence on safety and effectiveness of treatments in real life (so-called “real-world evidence”), especially based on routinely collected data. Use these data to compare effectiveness and cost-effectiveness of treatments and influence care processes, complementing information collected from clinical trials.
- Regularly update provider payment schedules and introduce ad-hoc payments, as necessary, to encourage adoption of value-adding and cost-effective technologies.
- Rebalance negotiating powers of payers and manufacturers in the pharmaceutical sector. This could be achieved through increased transparency and cooperation between payers and international joint procurement initiatives – tested in Europe and Latin America. In the case of oncology, innovative pricing methods could be developed, such as bundled or indication-based payment. Performance-based pricing agreements (used in Italy and England) should be applied parsimoniously to avoid high administration costs and make sure that new evidence generated is made available to the community.
- Re-assess orphan drug legislation to make sure incentives are not diverted from their initial vocation to encourage R&D investments in areas that would not be explored otherwise.

### **Harness the potential of health data while managing risks appropriately**

- Implement sound, fit-for-purpose governance frameworks to make the most of health data, while managing the risks appropriately. While no country has, to date, implemented the ideal information infrastructure and health data governance, potential models for harnessing opportunities include Denmark, Finland, Iceland, Israel, Korea, New Zealand, Norway, Singapore, Sweden and the United Kingdom (England and Scotland).
- Ensure strong data governance and technical and operational readiness to capitalise on the opportunity presented by Electronic Health Record (EHR) systems. A recent OECD survey suggests that Canada, Denmark, Finland, New Zealand, Singapore, Sweden, the United Kingdom (England and Scotland) and the United States are advanced in putting EHR data to work.



## Essential medicines for universal health coverage

Wirtz VJ, Hogerzeil HV, Gray AL, Bigdeli M, de Joncheere CP, Ewen MA, et al. 2016

### Essential medicines for universal health coverage



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#### Executive summary

Essential medicines satisfy the priority health-care needs of the population. Essential medicines policies are crucial to promoting health and achieving sustainable development. Sustainable Development Goal 3.8 specifically mentions the importance of “access to safe, effective, quality and affordable essential medicines and vaccines for all” as a central component of Universal Health Coverage (UHC), and Sustainable Development Goal 3.b emphasises the need to develop medicines to address persistent treatment gaps.

The recognition of the importance of essential medicines is not new. At the 1985 Nairobi Conference on the Rational Use of Drugs, government representatives and other stakeholders proposed a comprehensive set of essential medicines policies. 30 years later, *The Lancet's* Commission on Essential Medicines Policies convened to explore these questions: what progress has been achieved? What challenges remain to be addressed? Which lessons have been learned to inform future approaches? And how can essential medicines policies be harnessed to promote UHC and contribute to the global sustainable development agenda? This report addresses these questions, with the intent to reposition essential medicines policies on the global development agenda.

The Commission identified five areas that are crucial to essential medicines policies: paying for a basket of essential medicines, making essential medicines affordable, assuring the quality and safety of medicines, promoting quality use of medicines, and developing missing essential medicines. The Commission located essential medicines policies within the context of current global debates about balancing trade and intellectual property policies with human rights, assuring health security, strengthening people-centred health systems, and advancing access to essential technologies. In all policy areas, particular attention was paid to furthering equity in access, strengthening relevant institutions, and creating accountability. For each policy area, the Commission made actionable recommendations, thereby reaffirming essential medicines policies as a central pillar of the global health and development agenda.

#### Paying for a basket of essential medicines to promote sustainable access for all

Globally, a quarter of all health expenditure is on medicines. In many countries, the main source of financing for medicines is direct payment by the individual and households—this source is both highly

inequitable and inefficient, and its reduction is a key target for UHC. Furthermore, the Commission found that the available data on pharmaceutical expenditure in many countries lack sufficient detail on the types of medicines procured or sold, public and private sector spending, and the degree of access by key population subgroups.

For this report, the Commission developed a new model-based global estimate of the total financing that would be needed to achieve universal access to a basic package of essential medicines in low-income and middle-income countries (LMICs). A costing model was developed on the basis of disease prevalence, current or projected consumption of medicines, and international reference prices. Using two consumption scenarios, the Commission estimated that between US\$77.4 and \$151.9 billion (or \$13 to \$25 per capita) is required to finance a basic package of 201 essential medicines (378 dosage forms) in all LMICs. Yet in 2010, the majority of low-income countries (LICs) and 13 out of 47 middle-income countries, spent less than \$13 per capita on pharmaceuticals. Thus, the Commission confirmed that many people worldwide do not have access to even a limited basket of essential medicines. Countries should adapt the Commission's model to their national context to create a locally relevant estimate as a benchmark for measuring performance on essential medicines. The Commission's recommendations on financing of essential medicines are:

- Governments and national health systems must provide adequate financing to ensure inclusion of essential medicines in the benefit packages provided by the public sector and all health insurance schemes.
- Governments and national health systems must implement policies that reduce the amount of out-of-pocket spending on medicines.
- The international community must fulfil its human rights obligations to support governments of LICs in financing a basic package of essential medicines for all, if they are unable to do so domestically.
- Governments and national health systems must invest in the capacity to accurately track expenditure on medicines, especially essential medicines, in both the public and private sectors, disaggregated between prepaid and out-of-pocket expenditure, and among important key populations.

#### Making essential medicines affordable is necessary to achieve equity in access

The affordability of essential medicines is a core challenge for any health system working to achieve UHC,

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and therefore features prominently on the global agenda. The complexity of the problem of affordability illustrates the urgent need for comprehensive policy solutions; no single policy alone can solve this problem.

The lack of medicines pricing information makes it difficult for consumers—both individuals and health systems—to make informed decisions about purchasing medicines. Scarcity of data also impedes assessments of whether individuals and households face financial barriers when making out-of-pocket payments for medicines, and creates a barrier to cross-national comparisons that could inform the setting of benchmarks and the establishment of appropriate and effective pricing policies.

Medicines benefit packages guide procurement and reimbursement for affordable essential medicines. Compiling these packages necessitates building capacity at national level to translate findings from evidence (including health technology assessments) to local contexts, and to use the findings as inputs in decision making (including when to intervene to influence pricing). Governments and other purchasers of medicines can expand their transparent sharing of information to increase efficiency and avoid duplication of efforts.

The Commission's recommendations on making essential medicines affordable are:

- Governments and health systems must create and maintain information systems for routine monitoring of data on the affordability of essential medicines, as well as price and availability, in the public and private sectors.
- Governments must implement a comprehensive set of policies to achieve affordable prices for essential medicines.
- Governments and health systems must develop national capacity to create medicines benefit packages that guide procurement and reimbursement for affordable essential medicines.
- Governments, national health systems, and the pharmaceutical industry must promote transparency by sharing health and medicines information.

#### Assuring the quality and safety of medicines is needed to prevent harm to patients

Despite impressive progress, serious problems with medicine quality and safety remain, particularly in LMICs. These problems threaten the health of people and waste resources. Quality and safety of medicines are compromised when manufacturers, whether by accident or intent, produce substandard products, and when the supply chain allows unsafe, and sometimes dishonest, practices during transport and delivery. Current regulatory capacity and enforcement are insufficient in most LMICs.

Global and national regulatory structures therefore require considerable and urgent reform to assure the

quality and safety of medicines. The large donor programmes for AIDS, tuberculosis, and malaria treatments have helped to advance strategies on quality procurement, such as the WHO/UN Prequalification Programme. A clear trend towards international regulatory collaboration and electronic communications has emerged. These trends can now be leveraged to ensure continued progress for the full array of essential medicines for all countries.

The Commission's recommendations on assuring the quality and safety of essential medicines are:

- Global efforts must be made to promote the harmonisation of quality assurance efforts through the use of an international standard regulatory dossier that covers both format and content.
- WHO should evolve the WHO/UN Prequalification Programme to maintain a moving focus on new essential medicines.
- Payers and procurement agencies must adopt good procurement practices that incorporate effective and transparent quality assurance mechanisms.
- Governments must redirect the activities of national regulatory agencies towards those that add value and reduce duplication of effort, and engage with a system for independent and public assessment of the performance of NMRAs.
- Regulatory agencies must encourage the involvement of other stakeholders and the general public in promoting the quality and safety of essential medicines.
- WHO and national governments must establish concrete targets and a public accountability mechanism for the performance of national regulatory authorities.

#### Promoting quality use of essential medicines leads to better health outcomes and can achieve considerable efficiencies

Medicines can treat diseases and alleviate suffering, but only when a patient receives and takes the right medicine to treat the symptom or disease, in the right formulation and dose, at the right time, and for the right duration. When any of these conditions are not met, problems with medicines use ensue. These problems include overuse (as with opioids in some settings), underuse (as in many countries with poor access to opioids for the management of severe pain), misuse (as when antibiotics are taken for a viral disease), and unnecessarily expensive use (as when brand-name medicines are used despite the existence of a lower-priced, quality-assured generic alternative). As UHC enables more people to have access to medicines, problems with the use of medicines threaten to undermine the potential benefits by harming individuals, reducing the efficacy of medicines (if antimicrobial resistance develops), and jeopardising the financial stability of health systems.



Problems of inappropriate use do not arise from a single root cause—thus, addressing them requires complex and coordinated interventions. The Commission's recommendations focus on strategies that enable collaboration among patients, health-care providers, insurers, supply chain managers, and others (including the pharmaceutical industry), to incentivise and support quality medicines use. Strong institutions with the capacity to generate evidence and implement evidence-informed policies are crucial. The benefits of these efforts will include improving clinical, public health, economic, and ethical outcomes.

The Commission's recommendations on improving the use of essential medicines are:

- Governments and the main public or private payers should establish independent pharmaceutical analytics units (or equivalent) to focus on generating information for action to promote quality use, in conjunction with other objectives.
- Pharmaceutical analytics units must collaborate with multiple stakeholders in all relevant systems to increase their engagement in and accountability for quality use of medicines, and to intervene jointly on medicines use problems.
- Engaged stakeholder groups, led by data produced by the pharmaceutical analytics unit, should identify and prioritise local medicines use problems, identify contributing factors across the system, and develop and implement sustainable, long-term, multi-faceted interventions.

#### **A global research and development (R&D) policy framework is needed to develop missing essential medicines and make them accessible to all**

The present system for developing medicines is in crisis, largely failing to produce much needed products that address the health needs of millions of people worldwide. The prices of new essential medicines that are developed are sometimes so high that even high-income countries face financing problems. Pharmaceutical companies and their shareholders are typically reluctant to invest in marketing medicines for patient populations that do not represent a profitable market. These two problems are related, and disproportionately affect people in LMICs.

With the current patient-based innovation system, the feasibility of achieving or maintaining UHC is seriously at risk. Several not-for-profit initiatives, often in collaboration with the pharmaceutical industry, have compensated for some problems with the current system, but they do not represent a long-term solution. A new global policy framework is needed to drastically adapt the current model and to reduce its reliance on market exclusivity as the main driver of innovation. Governments need to define a list of missing essential medicines to be provided under UHC schemes, and governments, non-governmental organisations, and the industry need to make the necessary R&D financing

mechanisms available for these identified needs. The price of new essential medicines can then be delinked from development costs and the products can be made widely available and affordable through non-exclusive licensing agreements. The resultant decrease in price can provide the financial space to more directly finance the identified priority R&D.

The Commission's recommendations on developing missing essential medicines are:

- Governments and WHO must take international public leadership for priority setting for essential R&D, with due regard for the public health needs of LMICs.
- Governments must lead the process towards a global research and development policy framework and agreements, which include new financing mechanisms to ensure that missing essential medicines are developed and made affordable.
- The international community must create a general Essential Medicines Patent Pool.
- Governments and national stakeholders must develop and implement comprehensive national action plans to guarantee equitable access to new essential medicines.
- The pharmaceutical industry must better align its R&D priority setting with global health needs, and develop access strategies to make medically important innovations available to all in need.

#### **Measuring progress holds all stakeholders accountable**

The Commission's recommendations represent a compilation of proven and promising practices to improve national policies to assure access to quality-assured, affordable essential medicines and their quality use as a general component of UHC. To transform these recommendations into reality will require commitments on the part of governments, policy makers, implementers, the pharmaceutical industry, donors, health-care providers, citizens, and patients, as well as international agencies and civil society organisations. This commitment can be created in part through deliberate steps to document efforts and demonstrate progress. Thus, the Commission proposes a set of 24 core indicators to measure progress in the implementation of comprehensive essential medicines policies.

Together, the proposed indicators can track the progress of countries and the global community in their efforts to advance in the five priority areas for essential medicines policies (financing, affordability, quality and safety, use, and development of new medicines). The Commission intends these indicators to serve as a starting point for the continued development of accountability mechanisms that incorporate independent reviews and corrective actions. Setting appropriate targets for each indicator will be a crucial component of the process, requiring the active involvement of relevant stakeholders. National leadership, and promoting national ownership of results, should be a priority and



#### Panel 1: Sustainable Development Goals related to essential medicines

Sustainable Development Goal (SDG) 3 is: "Ensure healthy lives and promote well-being for all at all ages." Two targets for Goal 3 specifically mention essential medicines:

- SDG 3.8: "Achieve universal health coverage, including financial risk protection, access to quality essential health-care services, and access to safe, effective, quality and affordable essential medicines and vaccines for all."
- SDG 3.b: "Support research and development of vaccines and medicines for the communicable and non-communicable diseases that primarily affect developing countries, provide access to affordable essential medicines and vaccines, in accordance with the Doha Declaration...which affirms the right of developing countries to use to the full the provisions in the Agreement on Trade-Related Aspects of Intellectual Property Rights regarding flexibilities to protect public health, and, in particular, provide access to medicines for all."

For more on Sustainable Development Goal 3 see <https://sustainabledevelopment.un.org/sdg3>

lead to regional and global data sharing, making local data a global public good.

Accountability will allow governments, global agencies, the pharmaceutical industry, civil society organisations, other institutional stakeholders, and citizens around the world to track progress made on essential medicines policies to support UHC. This tracking will enhance other ongoing processes to measure and document progress towards the Sustainable Development Goals and national targets.

Without essential medicines, health systems cannot truly help people who fall ill, live with chronic disease, and go through various stages of life and death. Without strong health systems, populations cannot realise their right to health. 30 years after the first international conference on medicines policies, essential medicines are still essential. The Commission presents this report in the strong belief that the world can get essential medicines right, promoting improved performance and equity in health systems, while supporting UHC and enabling sustainable development.

#### Introduction

Essential medicines are central to promoting health and ensuring sustainable development. The Sustainable Development Goals (SDGs) adopted in September, 2015, by the member states of the UN recognise that equitable access to affordable, quality-assured essential medicines is a crucial step in achieving these key development targets (panel 1).<sup>1</sup>

Countries have agreed to move towards universal health coverage (UHC).<sup>2</sup> The aim of UHC is to "ensure that all people obtain the health services they need without suffering financial hardship when paying for them."<sup>3</sup> SDG 3.8 specifically mentions the importance of "access to safe, effective, quality and affordable essential medicines and vaccines for all."<sup>4</sup> Throughout this report, the phrase access to essential medicines denotes a broad definition, also used in SDG 3.8, which encompasses the quality, safety, and efficacy of medicines and vaccines, as well as their availability, affordability, and appropriate use.

Assuring access to essential medicines is crucial for moving towards UHC. This report presents the findings of the *Lancet* Commission on Essential Medicines Policies, which examined five core challenges that every country must address to secure access to essential medicines.

#### Five core challenges for essential medicines policies

Adequate financing to pay for an appropriate set of essential medicines is the first key challenge. Medicines represent a large proportion of household expenditure on health in low-income and middle-income countries (LMICs).<sup>5</sup> According to the World Health Survey, up to 9-5% of the total expenditure of poorer households in LMICs is spent on medicines, far higher than the 3-5% expended by poorer households in high-income countries (HICs).<sup>6</sup> This statistic is particularly true in countries where inadequate public financing of health care results in high out-of-pocket expenditure.<sup>7</sup> Little evidence exists to indicate how much financing would be required to pay for essential medicines for all.

The focus of the second challenge is affordability of essential medicines, as determined by comparing the price of the product to the amount the buyer can afford. High prices for medicines are often associated with the period of monopoly under patent protection. However, even lower-priced medicines can become unaffordable to most households in low-income countries (LICs).<sup>8</sup> Affordability becomes a particularly serious problem when medicines are needed for chronic conditions, including non-communicable diseases (NCDs). Affordability of medicines has become a key issue for governments, as well as public and private payers for health care, regardless of a country's income level. European countries affected by the global financial crisis have reported restricted access to essential medicines.<sup>9</sup> In the USA, state-funded health-care institutions that are responsible for prisoners have been sued over the poor access to new high-priced essential medicines for hepatitis C.<sup>10</sup>

The third key challenge is assuring the quality and safety of essential medicines. Poor-quality medicines seriously undermine the effectiveness of health care, as well as public confidence in the health system. Many incidents of harm from sub-standard and falsified medicines have been recorded.<sup>11,12</sup> For example, poor-quality antimalarial medicines are responsible for an estimated 122,000 deaths per year in children under 5 years in 39 sub-Saharan African countries.<sup>13</sup> Contaminated medicinal products were responsible for the deaths of more than 100 children in Panama<sup>14</sup> and 230 patients in Pakistan.<sup>15</sup>

Medicines cannot have a positive impact on health unless they are used appropriately. Nominal health coverage of a population is not sufficient to ensure quality use of medicines. Multiple factors contribute to the problems of overuse, underuse, incorrect use, and unnecessary



**Drug Regulation and Pricing — Can Regulators Influence Affordability?**

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## Drug Regulation and Pricing — Can Regulators Influence Affordability?

Hans-Georg Eichler, M.D., Hugo Hurts, M.Sc., Karl Broich, M.D., and Guido Rasi, M.D.

Public debate in the 1990s over drugs' clinical toxicity has given way to concerns about their financial toxicity. Although drug regulators aren't supposed to be concerned with pricing, they've been drawn into an acrimonious debate over the cost of medicines.

At the European Medicines Agency (EMA), we often hear conflicting arguments: high and inflexible regulatory standards drive up the cost of pharmaceutical research and development (R&D), thereby increasing drug prices; regulators license products even when the data are insufficient for assessing their value and allow drug makers to overcharge; more generics, biosimilars, and me-too drugs are needed to create a dynamic market that will keep prices down; me-too drugs should be discouraged, since they offer no added benefit to patients and lead to overutilization and higher spending; and regulators shouldn't allow drugs on the market that no one can afford.

So are regulators responsible for high drug prices? The short answer is yes and no. Before drug regulatory agencies existed, all sorts of "remedies" were sold on street corners — sometimes for a penny. But even if high prices weren't always an issue, concerns about product quality, safety, and lack of efficacy created a need for regulation. In the ensuing decades, regulatory agencies have developed sophisticated

evidence standards to ensure that approved drugs have favorable benefit-risk profiles. Regulators have, for example, developed rigorous standards for the generation and analysis of clinical trial data and for acceptable trial end points and study designs. Regulatory requirements have undoubtedly made pharmaceutical R&D expensive.

At the same time, a regulatory seal of approval is the most important distinguishing factor that allows drug developers to charge high prices for products. Without evidence that has been vetted by regulators, why would anyone pay more for any drug than they would for, say, a dietary supplement? If we eliminated regulation, the current biopharmaceutical business model would collapse — and so would science-based drug development. Without a requirement for regulatory approval, companies would have no incentive to conduct expensive clinical trials of their products. Lowering regulatory standards would be unwise for both patients and organizations that invest in pharmaceutical R&D. Robust regulation improves public health and creates economic value.

But the fact that regulation drives up R&D costs doesn't mean it's the only factor contributing to high prices — or even the most important one. Nor can we conclude the converse — that if only the high cost of R&D (driven by regulations) could be reduced, then prices would auto-

matically drop. Even pharmaceutical executives admit that this assumption is naïve; companies tend to charge whatever the market will bear. Any belief in a correlation between R&D costs and market price was dispelled during the recent debate over the price of the new hepatitis C drug Sovaldi.<sup>1</sup>

Regulators should not, for the sake of affordability, yield to pressure to lower standards. But it's also inappropriate for them to be oblivious to the growing budget pains caused by newly authorized products. We believe there are several ways regulators can contribute to keeping drug spending sustainable, at least in the European Union (EU). (We recognize that some of these steps may not be readily implementable in the United States, owing to its legislative framework.)

First, by rapidly approving generics and biosimilars and allowing them to enter the market once patents or exclusivity periods have expired, regulators can facilitate competition, which drives down prices. Regulators could, for example, fast-track additional generic authorizations when companies are taking advantage of monopoly conditions for generic drugs.

Second, regulators can work to ensure that me-too products continue to come on the market at a reasonable speed. Some consumer advocates lament the high proportion of me-too products



that provide limited or no added value over available drugs. But added value is difficult to predict, and some me-too products that were originally criticized have benefited patients and provided additional treatment options. More important, sometimes the availability of these products can drive down prices almost as much as the availability of generics. When hepatitis C medications similar to Sovaldi entered the market, for example, prices were reduced and access to treatment broadened.<sup>2</sup>

Third, regulators can encourage clinical trials that measure value. Payers need data that enable them to assess value in order to determine how much they

regulatory decision makers and support demonstration of value to payers.

Fourth, regulators can facilitate collection of other kinds of data that are important to payers. Increasingly, payers and pharmaceutical companies are considering outcome-focused deals tying a drug's price to the results achieved. Although pay-for-performance schemes are attractive in theory, practical hurdles have prevented widespread adoption. Most important is the difficulty of collecting and interpreting the relevant patient-level data in a given health care system. Regulators, at least in some countries, can facilitate data collection by con-

their R&D costs. When prices are squeezed, improving R&D efficiency will become even more important than it is today. How can regulators help achieve this goal?

Clinical drug development is generally an inefficient process. The cost of conducting clinical trials drives R&D spending, and much of the elaborate superstructure involved needs to be reassessed and could be pared down without harming participants. The EMA actively promotes better design and more efficient trial conduct<sup>4</sup> and supports the efforts of the Clinical Trials Transformation Initiative, created by the Food and Drug Administration and Duke University, and other efforts to streamline trials.

Similarly, conventional development and licensing pathways are often economically inefficient. Working with HTA bodies and patient groups, the EMA is exploring whether a more flexible development, licensing, and reimbursement approach called adaptive pathways may help companies stagger clinical development costs, generate revenue earlier, and remove some risk from R&D without relaxing the criteria for determining products' risk-benefit profiles.<sup>5</sup> We expect that this kind of "life span" approach to generating evidence — with more targeted selection of trial participants, managed growth of the treatment-eligible population, and full use of postlicensing Risk Management Plans (EU) or Risk Evaluation and Mitigation Strategies (United States) — will lower the threshold for financing drug development at a time when prices are coming under pressure.

We firmly believe that assessment of quality, safety, and effi-

***Regulators should not, for the sake of affordability, yield to pressure to lower standards. But it's also inappropriate for them to be oblivious to the growing budget pains caused by newly authorized products.***

should pay for a given drug. Health technology assessment (HTA) bodies that advise payers say that the clinical trials supporting marketing authorization often fall short in providing such data. The additional information required may relate to, for example, measures of quality of life or health care resource utilization. To bridge this gap, the EMA, and some EU member states, have been hosting "parallel scientific advice" sessions at which regulators, HTA experts, and drug developers discuss premarketing clinical trial designs. Experience from nearly 70 of these sessions shows that studies can generally be designed to satisfy the needs of

considering payers' needs when asking companies to conduct post-approval studies. In at least one case, a company was able to piggyback an outcomes-based scheme on processes already in place to monitor a drug's safety.<sup>3</sup> The EMA is now exploring with HTA bodies ways to collaborate on registries or other forms of post-approval evidence generation to achieve these dual goals.

It's clear that in the future, the market will not bear some of the higher drug prices that are being fetched today. One implication for public health is that potentially useful products may not be developed if companies fear they won't be able to recoup

cacy should remain separate from pricing and reimbursement decisions. Regulators alone cannot solve the growing problem of high drug prices. We understand that new drugs should command prices that reward and provide incentives for R&D investment. However, we fail to comprehend prices that, like Sovaldi's, recoup the entire investment within the first few months after a product's launch but are so unaffordable that patients in need are denied access.<sup>1</sup> We are committed to doing our part to facilitate continued access to effective and safe treatments.

The views expressed in this article are those of the authors and do not necessarily reflect those of the European Medicines Agency, its committees or working parties, or the national authorities with which the authors are affiliated.

Disclosure forms provided by the authors are available with the full text of this article at [NEJM.org](http://www.nejm.org).

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## The \$2.6 billion pill—methodologic and policy considerations

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### The \$2.6 Billion Pill — Methodologic and Policy Considerations

Jerry Avorn, M.D.

The introduction of several new astonishingly expensive prescription drugs has rekindled debate over the origins of and justifications for those prices. At a press conference in Boston last November, the

Tufts Center for the Study of Drug Development announced it had calculated that it costs pharmaceutical companies \$2.6 billion to develop a new drug<sup>1</sup> — up from the \$802 million the Center estimated in 2003. Because the new findings were presented at a media event that offered limited information regarding the methods used to arrive at this figure, it is difficult to know much about the solidity of the approach or the validity of the reported number. Before the findings could appear in the peer-reviewed literature, the figure was catapulted into the midst of the current hot debate about the pricing of many new drugs.<sup>2</sup>

Since the figure's release, it has been used to justify the cost of several expensive medications and to support longer periods of marketing exclusivity for new drug products. These arguments are based on the proposition that drug companies (which are major supporters of the Tufts center) must be helped to recoup the huge capital needs required to discover the cures of tomorrow.

The methods used to generate the \$2.6 billion figure will require careful scrutiny once they are available for detailed review. The analysis was based on data that 10 unnamed drug makers provided on 106 unnamed investigational compounds that they had “self-

originated.” The raw numbers on which the analysis is based are not available for transparent review — and are likely never to be divulged. The study included both products that made it to market and a much larger number that did not — a fair approach, since a balanced assessment would have to take into account the costs of failures as well as successes. But because we cannot know which compounds were studied, it is hard to evaluate the key assumption that more than 80% of new compounds are abandoned at some point during their development — a key driver of the findings.

Notably, as in the Center's previous estimates, nearly half the cost of drug development was accounted for not by research expenditures but by the cost of capital. The analysts justified that assumption by noting that during the years a company spends develop-



ing a new product, it incurs opportunity costs by not using those dollars for other purposes. That argument is plausible, and such calculations can be an appropriate component of such analyses. However, nearly half the total cost of developing a new drug (\$1.2 billion) was ascribed to this cost of capital, with only \$1.4 billion attributed to funds actually spent on research. These capital costs were assessed at 10.6% per year, compounded — despite the fact that bonds issued by drug companies often pay only 1 to 5%. In terms of access to capital, it's interesting to note that large drug mak-

stantial payments received from the federal government for other research activities, such as testing their products in children. Perhaps most important, because the calculations are based only on products that the companies described as “self-originated,” the \$2.6 billion figure does not consider drug-development costs borne by the public for the large number of medications that are based on external research that elucidated the disease mechanisms they address. One recent analysis showed that more than half of the most transformative drugs developed in recent decades had their origins in publicly fund-

The Tufts study did identify one aspect of drug development whose costs were actually lower than those in the Center's previous analysis: the time required for regulatory approval has been shortened somewhat. This finding is supported by extensive data showing that most regulatory bodies are impressively prompt in making approval decisions once the results of drug trials have been submitted by a manufacturer. The Food and Drug Administration is now particularly quick, reviewing drugs at least as rapidly as drug-regulatory bodies in many other countries and often more quickly. By contrast, the highest cost the Tufts researchers identified was that of the failure of compounds earlier in development because of unanticipated problems with safety, lack of efficacy, or both. This expensive weakest link points not to costly regulatory delay but to the limits of companies' ability to efficiently choose compounds for development and to identify adverse effects or limited efficacy earlier in the development process.

Of course, it is extremely expensive and risky to develop a new medication, and inevitably many promising new treatments will fail before they can be marketed. Pharmaceutical companies do invest heavily in the work needed to bring successful products to market and often in the underlying research on which those products are based. But as risky as drug development is, the pharmaceutical and biotech industries remain among the most profitable sectors of the U.S. economy and actually spend only a small fraction of their revenues on truly innovative research. Furthermore, some of the most important recent new medications

*Without knowing which drugs were included in the Tufts analysis, there is no way to know how many of the “self-originated” products also built on underlying basic science research whose costs were borne by the public.*

ers are among the U.S. firms with the highest amounts of profits held overseas. Two pharmaceutical companies are ranked third and fourth among all U.S. corporations in this regard: Pfizer (\$69 billion) and Merck (\$57 billion), respectively. Collectively, another eight drug companies reportedly have an additional \$173 billion of capital that is retained overseas, untaxed by the United States.<sup>3</sup> Such funds could potentially help with the cash-flow problem that plays such a large role in these estimated costs of drug development.

The Tufts calculations also explicitly do not take into account the large public subsidies provided to pharmaceutical companies in the form of research-and-development tax credits or sub-

ed research at nonprofit, university-affiliated centers.<sup>4</sup>

Without knowing which drugs were included in the Tufts analysis, there is no way to know how many of the “self-originated” products also built on underlying basic science research whose costs were borne by the public. In the debate over what it costs to bring a new drug to market and who should be compensated at what level to keep new-product pipelines full, this aspect of drug research and development must also be taken into account. The question of how best to fund such research is particularly relevant given that the current budget of the National Institutes of Health (NIH), in inflation-adjusted dollars, is at its lowest level in 15 years.<sup>5</sup>



were not developed by large drug manufacturers but were acquired through purchase of the biotech firms that discovered them. These, in turn, are often spinoffs based on the discoveries of NIH-funded university research laboratories. For example, Gilead Sciences did not invent its blockbuster treatment for hepatitis C, sofosbuvir (Sovaldi), which it priced at \$1,000 per pill. Rather, it acquired the product from a small company founded by the drug's inventor, a faculty member at Emory University, much of whose work on the usefulness of



An audio interview with Dr. Avorn is available at [NEJM.org](http://NEJM.org)

nucleoside viral inhibitors was federally funded. Gilead paid \$11 billion in late 2011 for the rights to market Sovaldi, an amount it totally recouped in its first year of sales after approval of the drug in late 2013.

We need an accurate determination of all the costs that go into the creation of a new drug,

to inform ongoing discussions about how best to foster such development and the most reasonable way of paying for truly innovative medications—especially given the proliferation of “specialty” drugs that can cost patients and payers as much as \$300,000 per year. These analyses will in turn require a broad-based and transparent reckoning of the costs of all the research and development that lead up to the creation of a new drug. Such a comprehensive accounting could well lead to policy decisions focused less on the need to replenish the capital of pharmaceutical companies and more on preserving the taxpayer-supported scientific sources of new drug discovery on which so many therapeutic advances depend.

Disclosure forms provided by the author are available with the full text of this article at [NEJM.org](http://NEJM.org).

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## Executive summary

**H**ealth care systems in OECD countries are better than ever at promoting improved health and longevity, yet they involve major budgetary commitments that countries struggle to keep in check. Pressure is ever-mounting to provide greater and more equitable access to quality care and new treatments to ageing populations.

A significant share of health spending in OECD countries is at best ineffective and at worst, wasteful. One in ten patients is adversely affected during treatment by preventable errors, and more than 10% of hospital expenditure is allocated to correcting such harm. Many more patients receive unnecessary or low-value care. A sizable proportion of emergency hospital admissions could have been equally well addressed or better treated in a primary care setting or even managed by patients themselves, with appropriate education. Large cross-country variations in antibiotic prescriptions reveal excessive consumption, leading to wasted financial resources and contributing to the development of antimicrobial resistance. The potential for generic medicines remains underexploited. Finally, a number of administrative processes add no value, and money is lost to fraud and corruption. Overall, existing estimates suggest that one-fifth of health spending could be channelled towards better use.

This report takes a systematic approach to: i) identifying ineffective and wasteful activities within health care systems; ii) analysing their causes and the actors involved; and iii) providing a catalogue of suitable countermeasures. Acknowledging the existence of ineffective spending and waste might not be easy for health workers, managers and even the politicians responsible for health care systems. But this report highlights the positive corollary to this difficult admission: opportunities exist to release resources within the system to deliver better value care. Cutting ineffective spending and waste could produce significant savings – for policy makers struggling to cope with ever-growing health care expenditure, the opportunity to move towards a more value-based health care system is one that must be pursued decisively.

This report pragmatically deems as “wasteful”: i) services and processes that are either harmful or do not deliver benefits; and ii) costs that could be avoided by substituting cheaper alternatives with identical or better benefits. Linking actors – patients, clinicians, managers and regulators – to key drivers of waste – errors and suboptimal decisions, poor organisation and co-ordination, incentives misaligned with health care system goals, and intentional deception – helps to identify three main categories of wasteful spending:

- Wasteful clinical care covers avoidable instances when patients do not receive the right care. This includes duplicate services, preventable clinical adverse events – for instance, wrong-site surgery and many infections acquired during treatment – and low-value care – for instance, medically unnecessary caesarean sections or imaging.



- Operational waste occurs when care could be provided using fewer resources within the system while maintaining the benefits. Examples include situations where pharmaceuticals or medical devices are discarded unused or where lower prices could be obtained for the inputs purchased (for instance, by using generic drugs instead of originators). In other instances, costly inputs are used instead of less expensive ones, with no additional benefit to the patient. In practical terms, this is often the case when patients seek care in emergency departments, end up in the hospital due to preventable exacerbation of chronic disease symptoms that could have been treated at the primary care level, or cannot be released from a hospital in the absence of adequate follow-on care.
- Governance-related waste pertains to resources that do not directly contribute to patient care. This category comprises unneeded administrative procedures, as well as fraud, abuse and corruption, all of which divert resources from the pursuit of health care systems' goals.

All OECD countries are already seeking to tackle waste. At least 10 countries produce atlases to identify variations in health care activities that may not be medically justified, and 19 countries use Health Technology Assessment (HTA) to help determine the value of some new treatment options. Nearly half of OECD countries are actively striving to promote greater prescription of generic drugs. At least 14 countries have strengthened access to primary and community care services to divert inappropriate visits from emergency departments. To date, though, only a few have set up comprehensive and transparent adverse event reporting systems, which encourage learning and foster prevention of future problems, or systematic approaches to detecting fraud and abuse. Overall, significant opportunities still remain for more systematic efforts.

Better information is key. Generating and publishing indicators (such as those on unnecessary or low-value care, overprescription of antibiotics, and delayed hospital discharges) is required to bring the scale of the problem to the attention of a wider public. Today, no country can report on the unnecessary use of magnetic resonance imaging for low back pain and only five can link antibiotic prescription to diagnostics. Data on delayed discharges are available for only three countries. Such data are needed to inform policies to target waste through regulations, incentives, and organisational and behavioural changes.

Sustainable change can be achieved if patients and clinicians are persuaded that the better option is the least wasteful one. Approaches such as the *Choosing Wisely*<sup>®</sup> campaign illustrate what is possible. This clinician-led initiative aims to reduce low-value care by encouraging patient-provider conversations about whether specific services truly add value. It is now active in at least a third of OECD countries. Changing habits is often a necessary and key way to tackle waste – whether to improve adherence to clinical guidelines, increasing the safety of care, or to convince patients not to rush to the emergency department or request antibiotics at the first sign of a cold.

Incentives also matter. Policy makers should create an environment that rewards provision of the right services rather than their quantity – for example, by moving towards payment systems that promote value for patients across the stages of care delivery. As many as a third of OECD countries already seek to reward different types of providers for results achieved rather than for the number of interventions. To reduce the incidence of unnecessary health care services and wasteful failures in co-ordination, a handful of payers, most notably in the United States but also in Sweden, Portugal and the Netherlands, have moved towards bundled or population-based payments, with some promising results.

In addition, direct interventions to prompt organisational changes and co-ordination among providers are required to reduce wasteful spending. Good practice examples include the development of explicit discharge planning – seen in at least five countries – or the joint procurement of hospital pharmaceuticals. Many revolve around ICT-enabled sharing of information among different stakeholders – although efforts to develop a more complete picture of the full care pathways can be impeded by inadequate health data governance frameworks. Finally, regulation can have a role to mandate or expand desired practices – such as the use of HTA in coverage decisions, or accreditation to impose safety standards – or to ban undesired ones – for instance, self-referrals or inappropriate marketing.

Strategies to reduce waste can be summed up as: i) stop doing things that do not bring value; and ii) swap when equivalent but less pricy alternatives of equal value exist. While these solutions may not always require profound remodelling of health care systems, they do involve investment and behavioural changes. Substantial room exists to release resources by tackling health care system waste across the OECD.



## The Pharmaceutical Pricing and Reimbursement Information (PPRI) initiative–Experiences from engaging with pharmaceutical policy makers

Vogler S, Leopold C, Zimmermann N, Habl C, de Joncheere K. 2014

Article published in Health Policy and Technology, reporting about activities of the PPRI network

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### Abstract

*Objective:* To present the Pharmaceutical Pricing and Reimbursement Information (PPRI) initiative, as an illustrative example of an engagement with policy makers in the field of pharmaceutical pricing and reimbursement.

*Methods:* The paper is based on internal assessments and feed-back from the involved policy makers as well as an external evaluation.

*Results:* PPRI is a network of around 70 institutions, mainly public authorities for pharmaceutical pricing and reimbursement information from 41, mostly European, countries. It evolved from a European Commission co-funded project in 2005-2007 into a self-funded Member States borne initiative. The first years of PPRI were characterized by trust-building and developing a joint understanding and language. In the initial stages, country reports, so-called 'Pharma Profiles', written by policy makers, were among the most important deliverables. In the course of time, ad-hoc queries which require immediate, brief and precise answers have gained importance. PPRI is predominantly an internal network for and with policy makers; it is not a policy-making body.

*Conclusions:* After nearly one decade of existence, the PPRI network appears to be a sustainable network. Policy makers are committed to provide and share data and to contribute to the network as they have an added value for their daily work from access to evidence and the exchange of information and experience with fellow colleagues from other countries.

**Report of the United Nations Secretary General's  
High-Level Panel on Access to Medicines.  
Promoting innovation and access to health technologies**



United Nations Secretary General's High-Level Panel on Access to Medicines. 2016



## EXECUTIVE SUMMARY

In September 2015, 193 Member States of the United Nations adopted the 2030 Agenda for Sustainable Development (2030 Agenda). This agenda includes Sustainable Development Goal (SDG) 3 that aims to ensure healthy lives and promote the well-being of all people of all ages. SDG 3 is an important vehicle for realizing the right to health and the right to share in the benefits of scientific advancements, whose affirmation dates back to the Charter of the United Nations (1945), the Universal Declaration of Human Rights (1948) and the Constitution of the World Health Organization (WHO) (1948). These rights are also enshrined in the International Covenant on Economic, Social and Cultural Rights (1966) and various other international treaties, declarations and national laws, including at least 115 constitutions.

Consistent with the vision of the 2030 Agenda and a recommendation by the Global Commission on HIV and the Law that the United Nations Secretary-General establish a high-level body to propose ways of incentivizing health technology innovation and increasing access to medicines and treatment, Secretary-General Ban Ki-moon, in November 2015, announced the appointment of a High-Level Panel on Innovation and Access to Health Technologies.

In keeping with the commitment of United Nations Member States to enhance policy coherence for sustainable development, the High-Level Panel's terms of reference called for it to "review and assess proposals and recommend solutions for remedying the policy incoherence between the justifiable rights of inventors, international human rights law, trade rules and public health in the context of health technologies," among other things. In accordance with the principle of universality that underpins the 2030 Agenda and its aspiration to leave no one behind, the High-Level Panel views innovation and access to health technologies as a multi-dimensional and global problem that affects all countries.

### Health technology innovation and access

Over the last few decades, medical innovation has dramatically improved the lives of millions of people across the globe. Vaccines have significantly reduced the prevalence of diseases, ranging from polio to human papillomavirus. Antiretroviral medicines have greatly improved the lives of people living with the Human Immunodeficiency Virus (HIV). Personalized strategies based on molecularly-targeted medicines are likely to become central to cancer treatment in the future. Despite this noteworthy progress, millions of people continue to suffer and die from treatable conditions because of a lack of access to health technologies.

Investment in research and development (R&D) of health technologies does not adequately address a number of important health needs. In some cases, the cause lies in inadequate resourcing of R&D for diseases where the market does not provide sufficient return on investment. Antibiotics typically offer little pecuniary reward for years of often costly research. In these circumstances, experts warn that drug-

resistant viruses, bacteria, parasites and fungi could cause 10 million deaths a year worldwide by 2050. The current model of medical innovation is ill-equipped to respond to the increasing emergence of infectious diseases, such as Ebola and Zika. Meanwhile, neglected tropical diseases (NTDs) continue to receive inadequate funding for R&D and access to health technologies, despite more than a billion people living with one or more NTD. The situation is driven by the relatively low purchasing power of people disproportionately affected by such conditions.

There are many reasons why people do not get the healthcare they need, including, *inter alia*, under-resourced health systems, a lack of sufficiently qualified and skilled healthcare workers, inequalities between and within countries, regulatory barriers, poor health education, unavailability of health insurance, exclusion, stigma, discrimination and exclusive marketing rights. The High-Level Panel acknowledges the importance of addressing these multiple determinants to health technology innovation and access. However, the High-Level Panel's mandate is focused on one aspect of a complex challenge: the incoherencies between international human rights, trade, intellectual property (IP) rights and public health objectives.

Policies and agreements related to human rights, trade, intellectual property rights and public health were developed with different objectives at different times. State obligations include duties not only to respect, but to protect and fulfil the right to health. This requires taking proactive measures to promote public health. As reaffirmed by a recent Human Rights Council resolution, ensuring access to medicines, and particularly to essential medicines, is a fundamental element of these obligations. Trade rules and intellectual property laws were developed to promote economic growth and incentivize innovation. On the one hand, governments seek the economic benefits of increased trade. On the other, the imperative to respect patents on health technologies could, in certain instances, create obstacles to the public health objectives of World Trade Organization (WTO) Members.

The adoption of the WTO Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) in 1994 ushered in a new and unprecedented era of global intellectual property norms and created a new standard of intellectual property protection and enforcement. However, negotiators included safeguards, or 'flexibilities,' within the TRIPS Agreement that could be used by signatories to tailor national intellectual property regimes so that countries could fulfil their human rights and public health obligations (for instance, laws and regulations regarding competition, government procurement and medicines). The proliferation of free trade agreements containing expansive patent and test data protections on health technologies, which exceed the minimum standards for intellectual property protection required by the TRIPS Agreement (so-called 'TRIPS-plus' provisions), may impede access to health technologies. Also, an uneven application of health and trade policy within and among states can create tensions that fuel policy incoherence.



## Intellectual property laws and access to health technologies

Public health-sensitive intellectual property rules and mechanisms can help address the misalignment between profit-driven innovation models and public health priorities. Voluntary licences, entered into between right holders and third parties to facilitate the market entry of more affordable health technologies, have helped to lower treatment costs in many countries. TRIPS flexibilities – for example, the freedom to determine patentability criteria and further define concepts such as “novelty,” “inventive step” and “industrial applicability” – can ensure that patents are only awarded for genuine innovation. Similarly, the ability to determine the terms upon which compulsory licences are issued allows governments to fulfil their human rights obligations by securing the availability and affordability of health technologies. Many governments have not used the flexibilities available under the TRIPS Agreement for various reasons ranging from capacity constraints to undue political and economic pressure from states and corporations, both express and implied. Political and economic pressure placed on governments to forgo the use of TRIPS flexibilities violates the integrity and legitimacy of the system of legal rights and duties created by the TRIPS Agreement, as reaffirmed by the Doha Declaration. This pressure undermines the efforts of states to meet their human rights and public health obligations. The use of TRIPS flexibilities may also be impeded by the proliferation of bilateral and regional free trade agreements containing TRIPS-plus provisions.

The policies of public funders of health technology R&D can also play an important role in enhancing health technology innovation and access. The United States, for instance, holds a central position in health technology innovation. The country’s R&D and access policies influence other actors, including private and public sector donors and foundations, and have an impact on access to the fruits of technology worldwide. The introduction of the 1980 Bayh-Dole Act in the United States significantly changed academic research by allowing universities and public research institutions to patent the results of federally-funded research and license private enterprises to develop them. However, limiting access to academic discoveries can obstruct follow-on innovation and force taxpayers to pay twice for the benefits of publicly-funded research. Strong, enforceable policies on data sharing and data access should be a condition of public grants. Public funding agencies should strongly encourage patenting and licensing practices that benefit public health, including the use of non-exclusive licences, the donation of intellectual property rights, participation in public sector patent pools and other mechanisms that maximize innovation while promoting access. Open models of innovation can also lower entry hurdles and accelerate the pace of development of health technologies, including those needed to combat emerging infectious diseases.

## New incentives for research and development of health technologies

Market-driven R&D has been credited by some for producing a number of important health technologies that have improved health outcomes significantly worldwide. However, significant gaps in health technology innovation and access persist. Under the prevailing model, the biomedical industry, with the help of intellectual property and data protections, in addition to benefiting from public funding for research, recoups the costs of its R&D and marketing through high product prices protected by patent monopolies and data and market exclusivities. As a result, new technologies are rarely developed for health conditions which cannot deliver high returns, such as bacterial infections that only require antibiotics. Rare diseases that affect comparatively small proportions of the population have not traditionally attracted investments although this is changing.

Various efforts are being undertaken by governments, philanthropic organizations, international entities, civil society groups and the private sector to resolve the incoherence between market-driven approaches and public health needs. However, such efforts tend to be fragmented, disparate and insufficient to deal with priority health needs on a sustainable, long-term basis. A much greater effort must be directed to supplementing the existing market-driven system by investing in new mechanisms that delink the costs of R&D from the end prices of health technologies.

Identification of global health priorities is necessary to efficiently distribute scarce health resources, to substantially improve the health status of populations and to enhance global preparedness for future health crises. The current patchwork of public, private and philanthropic funding cannot sufficiently and sustainably improve access to health technologies. Greater and more sustainable financial commitments are needed from both the public and private sectors and should be coordinated to achieve maximum utility and effect.

## Governance, accountability and transparency

Good governance, strong and concrete accountability mechanisms and greater transparency are decisive enablers of the 2030 Agenda. An important factor behind the incoherence between human rights, trade, intellectual property and public health lies in the diverse accountability mechanisms and transparency levels of these different, but overlapping spheres. Trade- and intellectual property-related accountability mechanisms are typically regulated by the WTO Dispute Settlement Understanding and dispute settlement provisions found in free trade and investment agreements. In contrast, human rights and public health accountability mechanisms are characterized by varying and often limited degrees of precision, legal weight and enforceability.



Transparency is necessary to hold governments, the private sector and other stakeholders accountable for the impact of their actions on access to health technologies. However, accurate and comprehensive information on the costs of R&D, marketing, production and distribution, as well as the end prices of health technologies, can be difficult to aggregate. Existing public databases of health technology prices managed by international organizations and civil society groups, while laudable, tend to be limited in scope and accuracy, in part because of discounts, mark-ups, taxes and regional pricing differences. The absence of transparency in clinical trial data and a lack of coordination within national drug regulatory authorities can contribute to delays in the registration of new health technologies. Procurement decisions and generic manufacturing are often delayed by the absence of clear, accurate and up-to-date information on existing and expired patents. Moreover, trade and investment agreements containing TRIPS-plus provisions are often negotiated in secret. This lack of transparency makes it difficult to hold governments and other stakeholders accountable for the impact of their policies and actions on innovation and access to health technologies.

The incoherencies between the right to health, trade, intellectual property and public health objectives can only be resolved using robust and effective accountability frameworks that hold all stakeholders responsible for the impact of their decisions and actions on innovation and access to health technologies.

# Innovative payment models of high-cost innovative medicines

Expert Panel On Effective Ways Of Investing In Health. 2018

Report of the Expert Panel of effective ways of investing in Health (EXPH)

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## SUMMARY

The growth of pharmaceutical expenditures due to new high-cost innovative medicines, under the current institutional framework, creates financial challenges to health systems. The recognition that the current path of growth cannot be continued indefinitely leads to the search of new ways to ensure that innovation “that matters” is produced, that patients have access to innovation and that health systems are financially sustainable. This context leads to the discussion of innovative payment models for new medicines that improves the way the three above-mentioned objectives are met.

It is unlikely that a single payment model will be optimal for all situations. Some broad principles should be observed when defining specific payment models for innovative medicines and deciding on rewarding R&D in pharmaceutical products:

- Greater price and cost transparency, including the acknowledgement that high prices (high costs to payers) may or may not have underlying high costs of R&D.
- Revisit the promotion of innovation through patent law and market exclusivity, as other mechanisms to promote and reward high-value innovations can and should be devised. This is particularly true when clear areas of neglected attention can be identified in a consensual way. The patent system is the current best option for decentralized innovation efforts when consumers are price sensitive, but not necessarily otherwise. This opens space to explore new models of promoting innovation that will encompass novel payment models which may or may not be associated with different rules in R&D funding (say, making use of prize-awarding mechanisms).
- Develop methodologies to measure the social value of pharmaceutical products and systematically use such methods, for instance in the context of Health Technology Assessment.
- Have an assessment of exercise of market power in each price negotiation, as insurance protection set by health systems reduces the role of consumer’s price sensitivity in limiting price increases of new products under patent protection.
- Set better rewards for higher therapeutic value added, so that innovation efforts are directed to the more relevant areas.
- Payment systems should evolve in the direction of paying for acquisition of a service (treatment) and not of a product (pill).
- Explore non-linear payment systems, including bundling, price-volume agreements, differentiation across geographies, and across indications, ensuring the conditions required for all parties to benefit.
- Create dialogue platforms involving all relevant stakeholders.

**Keywords:** EXPH, Expert Panel on effective ways of investing in Health, scientific opinion, innovative payment models, high-cost medicines

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