



THE CONSEQUENCES OF GREATER NET PRICE TRANSPARENCY FOR INNOVATIVE MEDICINES IN EUROPE

Searching for a consensus

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AN EVIDENCE-BASED STUDY

Led by

Massimo Riccaboni
IMT School for Advanced Studies

Walter Van Dyck
Vlerick Business School

Co-Authored by

Pierre Bentata
Asterès and Y Schools

Pius Gyger
*Independent Consultant, previously member of
Swiss Federal Commission of Drugs*

Marcin Czech
Institute of Mother and Child

Joao Marques-Gomes
Nova University Lisbon

Wolfgang Greiner
Bielefeld University

Jorge Mestre-Ferrandiz
Universidad Carlos III Madrid

Wim Groot
Maastricht University

Luka Voncina
University of Rijeka

Prepared by:
Tim Wilsdon, Michele Pistollato, Kirsty Ross-Stewart
Charles River Associates
8 Finsbury Circus, London EC2M 7EA

Funded by:
Merck Sharp & Dohme (MSD)
2000 Galloping Hill Road
Kenilworth NJ 07033 U.S.A.

Authors

Massimo Riccaboni

*Professor of Economics
AXES Research Unit at IMT School for
Advanced Studies, Lucca, Italy*

Walter Van Dyck

*Associate Professor of Technology & Innovation
Management
Vlerick Business School, Belgium*

Pierre Bentata

*Associate Doctor of Economics
Asterès, Paris and Y Schools, Troyes, France*

Pius Gyger

*Health Economist
Independent Consultant, Switzerland
Previously member of Swiss Federal
Commission of Drugs*

Marcin Czech

*Professor
Institute of Mother and Child and Business
School, Warsaw University of Technology,
Warsaw, Poland*

Joao Marques-Gomes

*Assistant Professor
Nova School of Business and Economics, and
Nova Medical School, Portugal
CEO, JPMG*

Wolfgang Greiner

*Professor for Health Economics
Bielefeld University, Bielefeld, Germany*

Jorge Mestre-Ferrandiz

*Profesor Asociado
Universidad Carlos III Madrid, Spain
Independent Economics Consultant*

Wim Groot

*Professor of Health Economics
Maastricht University, The Netherlands*

Luka Voncina

*Assistant Professor
Faculty of Health Sciences, University of Rijeka,
Croatia
Independent Consultant, Freyr*

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Abbreviations

AIFA	Italian Medicines Agency	(Italy)
ASMR	Improvement of Medical Benefit	(France)
ATMP	Advanced therapy medicinal product	
CE	Cost-effectiveness	
CED	Coverage with evidence development	
CEPS	Economic Committee for Health Products	(France)
CPR	Price and Reimbursement Committee	(Italy)
DGFPS	Directorate of Pharmaceutical and Health Products	(Spain)
EFPIA	European Federation of Pharmaceutical Industries and Associations	
EMA	European Medicines Agency	
EKDF	Federal Commission for Drugs	(Switzerland)
EOPYY	National Organization for the Provision of Health Services	(Greece)
EU	European Union	
G-BA	Common Federal Committee	(Germany)
GDP	Gross domestic product	
GDPR	General Data Protection Regulation	
HTA	Health technology assessment	
INFARMED	National Institute of Pharmacy and Medicines	(Portugal)
IRP	International reference pricing	
MEA	Managed entry agreement	
MoH	Ministry of Health	
NGO	Non-governmental organisation	
NICE	National Institute for Health and Care Excellence	(England)
NPT	Net price transparency	
OECD	Organisation for Economic Co-operation and Development	
R&D	Research and development	
RWE	Real world evidence	
TA	Therapy area	
TLV	Swedish Dental and Pharmaceutical Benefits Agency	(Sweden)
UN	United Nations	
US	United States	
WHA	World Health Assembly	
WHO	World Health Organization	

WTP	Willingness to pay	
VBP	Value-based price	
ZIN	National Health Care Institute	(Netherlands)

Executive Summary

Introduction

The merits of greater or lesser net price transparency (NPT) has been a topic for discussion for many years across business and industry in general. However, in the past few years, the debate on NPT of innovative medicines has intensified, with organisations such as the United Nations (UN), the World Health Organization (WHO) and the Organisation for Economic Co-operation and Development (OECD) leading calls for greater transparency in the pharmaceutical sector, specifically focused on prices. In May 2019 the World Health Assembly (WHA) approved a resolution to support the greater public disclosure of prices and research and development (R&D) costs for both medicines and other health products supported by several European and non-European governments. To contribute to the international debate on the transparency of medicine prices in Europe, Merck Sharp & Dohme (MSD) asked Charles River Associates (CRA) to curate a panel of experts to develop evidence on the impact of greater NPT of innovative medicines. Professor Walter Van Dyck¹ and Professor Massimo Riccaboni² were asked by CRA to lead this research, supported by a wider panel of 10 experts from a range of European markets.

A structured literature review was first conducted to summarise the theoretical consequences of greater NPT. This was supplemented with a survey of national payers and payer experts³ from a range of European markets. This was used as pre-read information for an expert advisory board of 12 economic and health economic experts representing 12 countries selected to give a range of market sizes, national income and payer approaches. The debate and the consensus reached by the advisory board have been summarised in this report. In addition, a computational model has been developed by two key investigators to provide new, empirical evidence to illustrate the impact of NPT on different European markets.⁴

Putting the ‘net price transparency’ debate into context

There is a need for clarity on the definition of ‘net price transparency’, and in particular to distinguish this from the concept of ‘pricing transparency’ or ‘pricing process transparency’ (Table 1). It is generally agreed that transparency in decision-making (pricing process transparency) is beneficial to the functioning of the innovative pharmaceutical market as it supports good governance, enhanced decision-making and efficiency. The disclosure of net prices of innovative medicines (NPT) is a different debate. Greater NPT, referring to the disclosure of nationally agreed ex-factory prices (which are currently confidential in most European markets), has myriad potential economic ramifications that could significantly affect patients, payers and the industry. Some experts have suggested that instead of looking for greater price transparency, markets that do not

1 Associate Professor of Technology & Innovation Management, Vlerick Business School, Belgium

2 Professor of Economics; AXES Research Unit at IMT School for Advanced Studies, Lucca, Italy

3 National payers and payer advisors were representatives of the national public body responsible for HTA and/or pricing decisions.

4 Van Dyck, W., Riccaboni, M., & Swoboda, T. 2020. Pharmaceutical net price transparency across European markets: Insights from a Multi-Agent simulation model, Vlerick Policy Paper Series #13. Brussels, Belgium: Healthcare Management Centre, Vlerick Business School.

have effective pricing process transparency measures should focus on this to ensure they are not overpaying for medicines from a local value perspective.

Table 1: Definition of ‘pricing transparency’ vs ‘price transparency’

<u>Pricing</u> process transparency	Transparency of the process used to decide prices, aiming to ensure accountability of the reimbursement decision-making process
<u>Price</u> transparency	Transparency of the final ex-factory price level agreed between national payers and manufacturers, aiming to disclose any preferential rebates a payer may have achieved

Source: CRA

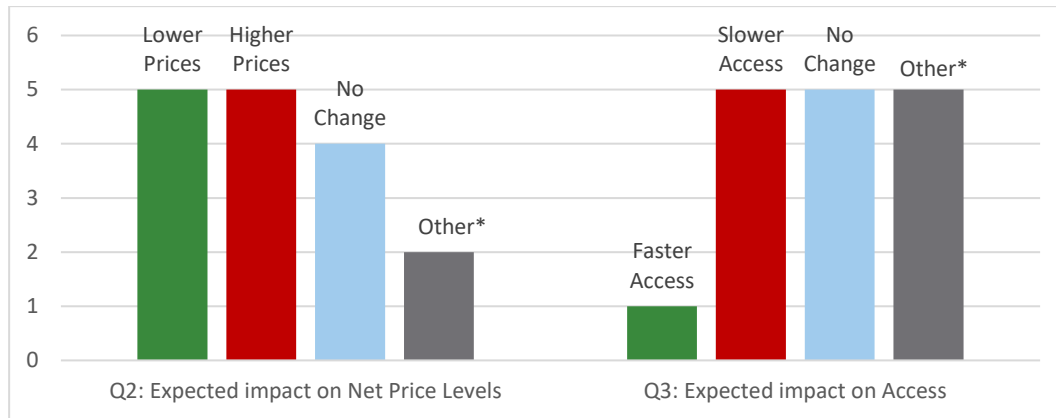
Calls for greater NPT should also be accompanied by more clarity on how to overcome practical challenges. For example, while there is often a price agreed between the manufacturer and the relevant national authority, this is rarely the price paid for an innovative medicine or the amount of money that the manufacturer receives. We note that there are many different prices associated to a single medicine: for example, there is the list price publicly disclosed by the manufacturer, the price including distribution margins and taxes, and several prices agreed with the national payer taking into account rebates, discounts, outcome-based payments and clawbacks. Further to this, the price can also vary depending on whether a product goes through a regional process or is subsequently negotiated at the hospital level. Calls for greater NPT also tend not to address other practical challenges flagged by experts during discussion, including the methods of information sharing (e.g. the channels through which the information is shared, who is responsible for sharing information and with whom the information should be shared) and how to account for current legislation that protects the confidentiality of pricing agreements.

The political view is not always fully aligned with payers regarding the consequences of NPT on national budgets

While many policymakers and payers express support for the concept of greater NPT, payers recognise the potential negative consequences of greater NPT without appropriate contingency measures. The views of many policymakers (which are made public and widely reported by the media) are largely supportive of greater NPT. This appears to be due to concerns around the prices of innovative medicines and perceptions of excessive profitability, together with a historically low level of trust in the pharmaceutical industry. The views of those responsible for negotiating prices on behalf of public health systems (payers) are less clear; therefore a survey with current and former payers and payer advisors was conducted to provide a basic understanding of these views. Insights from the payer survey indicated a more complex picture than is seen in the public domain for policymakers: although payers were generally supportive of greater NPT, expectations about the impact on price level varied significantly, and very few respondents indicated that they would expect any positive impact on patient access (Figure 1). Qualitative insights indicated that there were a number of drivers behind payer support of greater NPT. Firstly, survey respondents reported that there is a general attitude amongst payers to favour transparency, which is a concept with predominantly positive connotations. And secondly, payers tend to support equity across all European markets (whereas currently some are more transparent than others). Despite

this, results from the survey also indicated that payers have concerns about making their own prices transparent, underpinned by their belief that confidentiality allows for better prices to be achieved.

Figure 1: Payer expectations about the impact of greater NPT on net price levels and patient access (n = 16)



*Other: Respondents indicated that (a) they could not predict the outcome or (b) there would be a mix of outcomes (e.g. both higher and lower prices) dependent on current price levels and product characteristics.

Source: CRA Payer Survey (2020)⁵

There appears to be consensus that greater NPT will result in price convergence due to the frequent use of international reference pricing (IRP) mechanisms across European markets. In an environment where negotiators are able to reference prices in other markets, sellers would be more likely to offer all buyers similar prices in an effort to avoid a downward pricing spiral.⁶ There is some evidence to support this from other industries and through economic simulations that model increased transparency; for example, a recent simulation conducted for the medical devices space highlighted that all transparency measures resulted in the restricted ability of suppliers to sell at different prices to different hospitals.⁷ As a first consequence, greater NPT would therefore lead to more uniform prices.

It is also likely that price convergence will disproportionately affect lower-income markets. Although it is difficult to observe with any precision, the evidence suggests prices reflect affordability

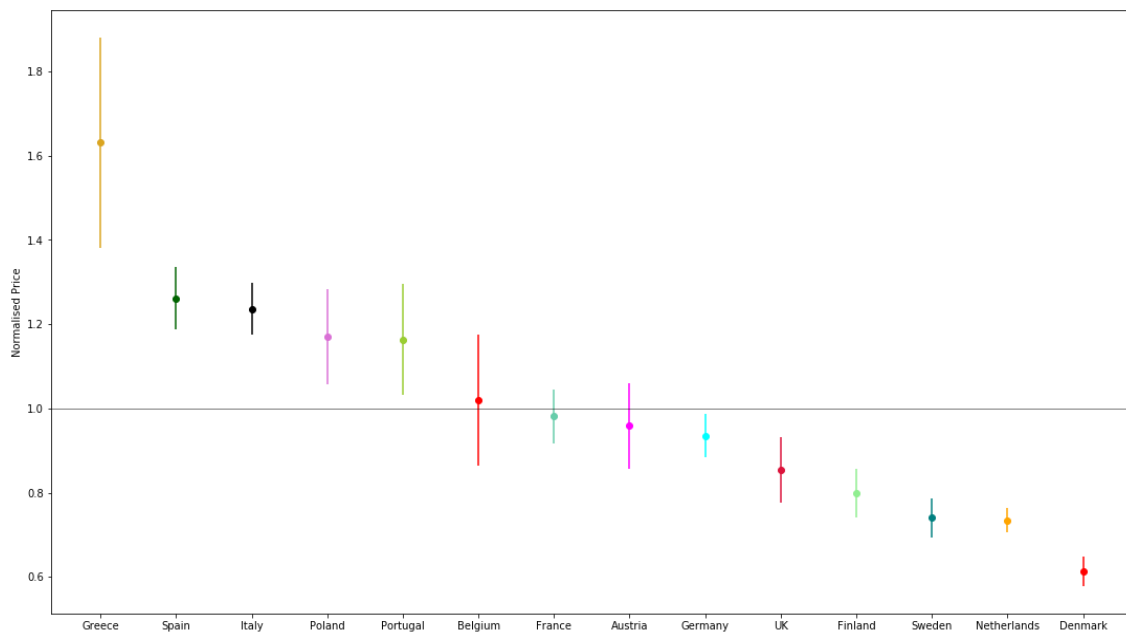
⁵ CRA Payer Survey. **Q2:** “What do you expect to happen (i.e. not what you would like to happen) to the prices of innovative medicines in your market, if the level of price transparency is increased in all European markets, including yours (so the confidential prices negotiated in your market are known to others) and, at the same time, assuming that pharmaceutical companies would strategically react to the disclosure of confidential agreements?”. **Q3:** What do you expect to happen (i.e. not what you would like to happen) to the time to access innovative medicines in your market, if: the level of price transparency is increased in all European markets, including yours (so the confidential prices negotiated in your market are known to others) and, at the same time, assuming that pharmaceutical companies would strategically react to the disclosure of confidential agreements?”.

⁶ Kyle, M.K. & Ridley, D.B. (2007). “Would Greater Transparency and Uniformity of Health Care prices Benefit Poor Patients?”. *Health Affairs*, 26 (5): 1384–1391. DOI 10.1377/hlthaff.26.5.1384

⁷ Grennan, M. (2013). “Price Discrimination and Bargaining: Empirical Evidence from Medical Devices”. *American Economic Review*, 103(1): 145–177. doi: 10.1257/aer.103.1.145

(as predicted by economic theory – Ramsey Pricing – and Differential Pricing principles).⁸ With price convergence, economic theory dictates that innovative medicine prices in markets that are paying below the European average will increase, while they could decrease in markets paying above the European average, typically the higher-income countries.⁹ As found in the computational model (Figure 2), lower-income markets could expect price increases under transparent conditions, whereas higher-income and low-volume markets could expect price decreases. At the extreme, some markets could see their prices increase by as much as 60%. It is also important to note that in cases where Ramsey pricing is not being adhered to (i.e. lower-income markets are paying more than higher-income markets), greater NPT might result in this situation being addressed, or at the very least changed so that prices are converged.

Figure 2: Normalised price change under NPT in selected European markets – a prediction from a simulation model



Source: Van Dyck, W., Riccaboni, M., & Swoboda, T. 2020. *Pharmaceutical net price transparency across European markets: Insights from a Multi-Agent simulation model*, Vlerick Policy Paper Series #13. Brussels, Belgium: Healthcare Management Centre, Vlerick Business School.

Greater NPT is expected to alter the functioning of the market for innovative medicines

⁸ Schweitzer, S.O. & Comanor, W.S. (2011). "Prices Of Pharmaceuticals In Poor Countries Are Much Lower Than In Wealthy Countries". *Health Affairs*, 30 (8)

⁹ Given the currently confidential nature of innovative medicine pricing, the computational model considers that the value-based price (i.e. price obtained without transparency/under normal conditions) is the average of the published list prices for a selection of innovative medicines over the period 1996–2008 with a normalised, average confidential rebate of 30% uniformly set for all countries. The model also assumes that in a transparent system, all markets will want to reference the lowest transparent price. See Van Dyck, W., Riccaboni, M., & Swoboda, T. 2020. *Pharmaceutical net price transparency across European markets: Insights from a Multi-Agent simulation model*, Vlerick Policy Paper Series #13. Brussels, Belgium: Healthcare Management Centre, Vlerick Business School for model details and robustness checks.

The use of IRP for price determination would increase with greater NPT, likely at the expense of health technology assessment (HTA) approaches. With greater emphasis during the price negotiation process being given to international medicine prices, the role of HTA in influencing pricing decisions is likely to change. As a result, greater NPT is expected to facilitate a shift away from value-based pricing (VBP) mechanisms that rely heavily on HTA and instead toward IRP mechanisms. Experts part of the advisory board also highlighted that this shift in price determination methodology could result in a situation where payers choose to determine innovative medicine prices based on whichever method allows them to achieve greater price reductions. In this situation, there is a danger that price setting becomes more delinked from the value a medicine delivers in a particular market, and also that the decision-making process behind pricing decisions becomes less transparent. Further to this, increased reliance on IRP ignores any differences in product use across markets and the differential value that one product can have in different markets (e.g. an anti-infective that is used in reserve in one market but needed earlier in the treatment paradigm in another due to higher epidemiology of resistant infections).

Experts also theorised that with greater NPT, some European markets would attempt to form coalitions and cross-country collaborations to put themselves in stronger negotiating positions and increase their bargaining power. Already, there are examples of cross-country collaborations across Europe applied to HTAs, reimbursement decisions and procurement, although none are used consistently for all medicine approvals (e.g. the BeNeLuxA-I coalition and the Valletta Declaration group). In theory these collaborations can be used to positive effect in the case of innovative medicines, particularly advanced therapy medicinal products (ATMPs), improving efficiency in assessment processes and decreasing time to access, but little empirical evidence of this currently exists. In an environment of greater transparency, countries could be forced to explore these alternative approaches more seriously as tools to gain efficient access to innovative medicines.¹⁰

An increase in NPT could in some cases lead to the misuse of pricing mechanisms. It has been suggested that markets may increasingly attempt to use complicated performance-based managed entry agreements (MEAs) to achieve an unobservable, ex-post discount. Today, MEAs are used for a variety of reasons, including providing financial discounts to payers but also providing more certainty to physicians and payers on the clinical impacts and/or cost-effectiveness (CE) of medicines.¹¹ The greater use of performance-based MEAs in order to circumvent requirements on NPT would be inefficient and not in line with the intended purpose of such agreements. In addition, markets with a lack of infrastructure or a lack of experience in implementing more sophisticated payment models could be unfairly disadvantaged by this misuse of MEAs since they will not have the same capabilities to achieve these proxy confidential discounts.

Greater NPT could adversely affect competition in the pharmaceutical market. The role of transparency in competition has been examined by academic and competition authorities.¹² It is important to notice the role that the degree of market concentration plays in the negative impact of increased price transparency: in more competitive markets, price transparency can deliver benefits

10 EFPIA (2019). "Policy Principles on Cross-country Collaborations on Medicines' Pricing and Access". Available at <https://www.efpia.eu/media/412513/policy-principles-on-cross-country-collaborations-on-medicines-pricing-and-access.pdf>

11 Klemp, M. and Frønsdal, K.B. (2011). "What principles should govern the use of managed entry agreements?" *International Journal of Technology Assessment in Health Care*, 27(1):77-83.

12 Austin, A., & Gravelle, J. (2007). "Does Price Transparency Improve Market Efficiency? Implications of Empirical Evidence in Other Markets for the Health Sector." Congressional Research Service.

to consumers in terms of increased competition; this has been the case, for instance, with digital platforms for online purchases. However, in industries facing a certain degree of market concentration (such as the innovative pharmaceutical industry), experience has shown that greater NPT can facilitate collusive behaviours, ultimately leading to higher prices. Further to this, greater NPT can be seen to disincentivise increased competition within a therapy area which could subsequently result in less pricing pressure on innovative products. Competition within a non-transparent market has frequently led to decreases in price and overall spending, for example in the case of Hepatitis C, where intense competition led to sharp decreases in prices and overall spending.^{13,14} Lastly, reduced competition following the implementation of price transparency measures has been seen in other industries, and although the pharmaceutical market is different, and lessons from other industries should be used with care, they should not be ignored.

The impact of NPT on patient access to innovative medicines

Access delays are likely and would be expected to affect patients in lower-income markets disproportionately. The presence of IRP mechanisms provides incentives for payers to delay price negotiations until prices in other markets are available. This also incentivises manufacturers to launch drugs in an order that will protect their prices.^{15,16} This occurs today, but NPT would amplify these incentives, thus increasing the potential access delays faced by markets with a lower price potential and, as predicted by the computational model, also in countries with a middle-level price.¹⁷ In these markets, it may be neither affordable for payers to agree to a higher price for a medicine nor possible for the industry to sustainably offer a lower price even if they wish to launch there (as illustrated in Figure 3). This may mean that pricing agreements in lower-income markets (vs highest-income markets) cannot be reached for several years until price erosion (e.g. caused by competitor entry in other markets) has brought the price to a level where they are able to pay.

Access delays are also likely to be largest for the most innovative products. There are a number of reasons why the value delivered by the most innovative medicines is likely to vary across countries (due to need for complementary healthcare infrastructure and diagnosis, for example). The asymmetry between the value and the volumes in the lower-income markets and higher-income markets is likely to be larger for these products. So, any impact of NPT will be exaggerated (given the commercial incentives to secure access in the higher-value/higher-volume markets). In this case, we might expect NPT to have a very strong impact on patient access, increasing the significant differences in access we already observe today. By this theory it is also true that for non-

13 Roediger, A., Wilsdon, T., Haderi, A., Pendleton, K. and Azais, B. (2019). "Competition between on-patent medicines in Europe". Available at <https://www.sciencedirect.com/science/article/pii/S0168851019301289>

14 Hawkes, N. (2019). "NHS England finalises procurement to eliminate hepatitis C". Available at <https://www.bmj.com/content/365/bmj.l1994.short>

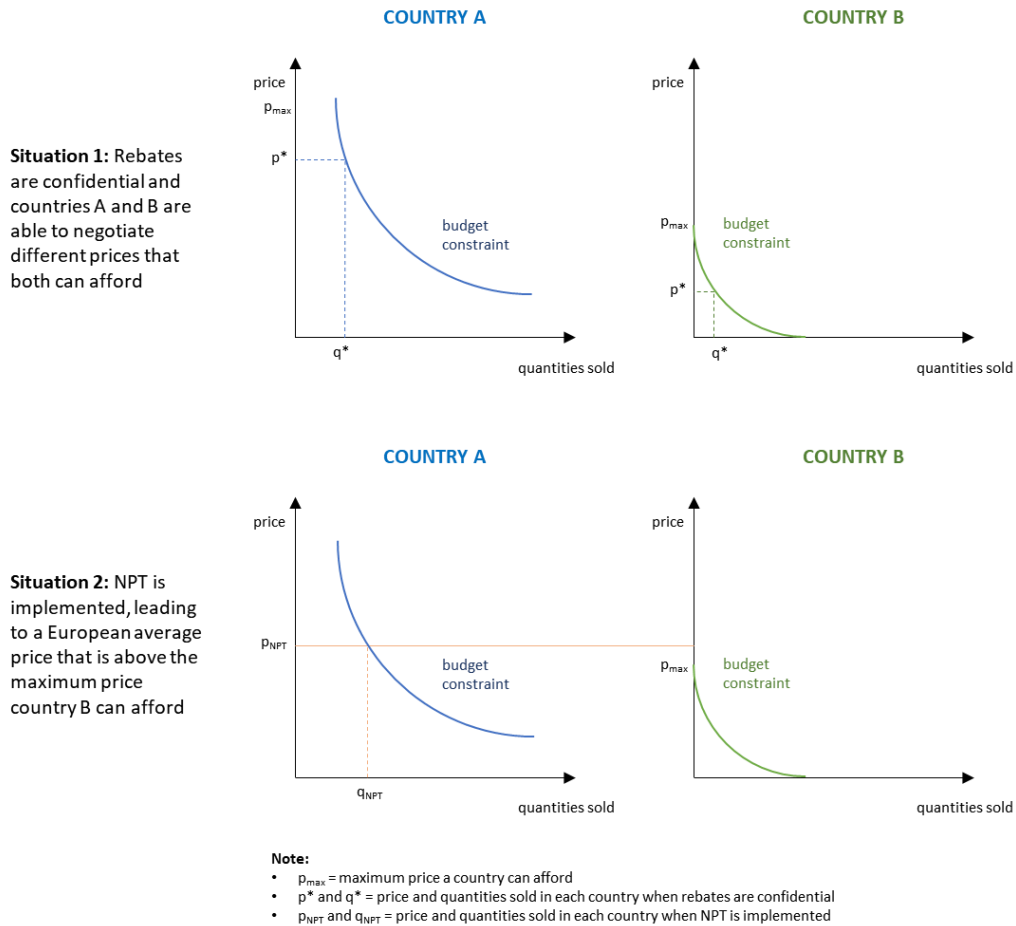
15 Zamora, B., Maignen, F., O'Neill, P. et al. (2019). "Comparing access to orphan medicinal products in Europe." *Orphanet J Rare Dis* 14, 95. Available at <https://doi.org/10.1186/s13023-019-1078-5>

16 Kanavos, P., Fontrier, A., Gill, J., & Efthymiadou, O. (2020). "Does external reference pricing deliver what it promises? Evidence on its impact at national level." *Eur J Health Econ* (21): 129–151. Retrieved 29 January, 2020, from <https://link.springer.com/article/10.1007/s10198-019-01116-4>

17 Van Dyck, W., Riccaboni, M., & Swoboda, T. 2020. Pharmaceutical net price transparency across European markets: Insights from a Multi-Agent simulation model, Vlerick Policy Paper Series #13. Brussels, Belgium: Healthcare Management Centre, Vlerick Business School.

innovative medicines, such as generics and biosimilars (not the focus of this white paper), greater NPT is likely to have less of an effect and potentially could even result in lower prices across markets. This is especially true of markets that do not now effectively use the available competition for these product types.

Figure 3: Price convergence means that markets with more stringent budget constraints will be kept out of the market and see increased delays to access



Illustrative representation: an accurate economic representation would consider additional market characteristics and dynamics (e.g. price elasticities, costs structure, price formation mechanism). However, the outcome from Situation 2 (i.e. no access in country B) represents an actual outcome that is possible under given circumstances.

Source: CRA Expert Advisory Board (2020).

Lastly, NPT could lead to considerable uncertainty and affect innovation. Although Europe only accounts for 23.3% of global pharmaceutical sales (2019 figures),¹⁸ greater NPT could impact prices in countries that reference European list prices (e.g. Australia, Canada and Japan); lower

18

EFPIA (2019). "The Pharmaceutical Industry in Figures: Key Data". Available at <https://www.efpia.eu/media/412931/the-pharmaceutical-industry-in-figures-2019.pdf>

prices in these markets could lead to reduced revenue and therefore to a reduction in capital available to re-invest in R&D. Similarly, with the Trump administration having made proposals for the use of IRP in the United States (US) for Medicare drugs,¹⁹ and the new administration continuing to show interest in IRP legislation,²⁰ this effect could be multiplied given the significant proportion of the market for which the US is responsible (the European Federation of Pharmaceutical Industries and Associations (EFPIA) reports that the US and Canada were responsible for nearly 50% of the pharmaceutical market in 2019).^{21,22}

Conclusions

The potential consequences of greater NPT in Europe show how important it is that policy regarding NPT is based on the economics of pharmaceutical pricing and is evidence-based.

In summary, there is a consensus across technical experts that greater NPT in Europe – as a single measure – is a risky and inefficient policy proposal to address issues in the healthcare system (without a level of solidarity between countries that would support differential pricing in the presence of NPT, that does not exist today). Although some advocates theorise that prices will decrease with greater NPT, an analysis based on economic theory shows that the picture is more complex, with significant associated risks for payer budgets and a danger of having the opposite impact in many markets, especially with regard to innovative medicines. Even if, in theory, greater NPT could lead to greater access to innovative medicines in high-income markets, this was not the opinion of the payers surveyed for this white paper. Only by bringing together a range of stakeholders to discuss the political and technical consequences of transparency will we be able to develop policy proposals that improve trust while maintaining efficiency in healthcare decision-making and patient access.

19 US Government website (2019). “Lower Prescription Drug Costs Now”. Available at: <https://www.speaker.gov/sites/speaker.house.gov/files/HR3%20Backgrounder%2010.2.19.pdf>

20 Joe Biden Website (2020). “Healthcare”. Available at <https://joebiden.com/healthcare/#>

21 EFPIA (2019). “The Pharmaceutical Industry in Figures: Key Data”. Available at <https://www.efpia.eu/media/412931/the-pharmaceutical-industry-in-figures-2019.pdf>

22 Dubois, P., Gandhi, A., & Vasserman, S. 2019. Bargaining and international reference pricing in the pharmaceutical industry, NBER Working Paper: University of Toulouse Capitole and Harvard University, Department of Economics

Table of Contents

1. Introduction	1
1.1. Background of the debate	1
1.2. Views of key stakeholders: policymakers, NGOs and the industry	3
1.3. A multifaceted methodology	6
1.4. Structure of the white paper	10
2. Putting the net price transparency debate into context	11
2.1. A definition of 'net price transparency'	11
2.2. The practical challenges associated to 'net price transparency'	12
3. The political view is not always fully aligned with payers regarding the consequences of NPT on national budgets	16
3.1. Differences in the political and payer views	16
3.2. Most payers expect there would be negative consequences from greater NPT	20
3.3. NPT will result in price convergence with negative consequences for national budgets, especially in lower-income countries	24
4. The impact of NPT on the functioning of the market for innovative medicines	30
4.1. Greater NPT would alter the way in which pricing mechanisms are applied	30
4.2. Greater NPT could encourage the misuse of payment mechanisms	32
4.3. Greater NPT could adversely affect competition in the pharmaceutical industry	34
4.4. Greater NPT could affect decision-making regarding international investments	36
5. The impact of NPT on patients access to different types of innovative medicines	38
5.1. Access delays are likely to differ across markets	38
5.2. Access delays are more likely for innovative products	40
5.3. Greater NPT could affect the development of new medicines	42
6. Conclusions	43

Table of Figures

Figure 1: Payer expectations about the impact of greater NPT on net price levels and patient access (n = 16).....	vii
Figure 2: Normalised price change under NPT in selected European markets – a prediction from a simulation model	viii
Figure 3: Price convergence means that markets with more stringent budget constraints will be kept out of the market and see increased delays to access	xi
Figure 4: Payers’ general support for greater NPT (n = 16)	17
Figure 5: Surveyed payers’ level of interest in each European market’s net price (1 = no interest; 5 = extremely high interest).....	19
Figure 6: Payer level of interest in the net price information from all European countries or a group of countries	20
Figure 7: Payer expectations about the impact of greater NPT on net price levels and patient access (n = 16).....	21
Figure 8: Simplified examples to illustrate the implications of abandoning differential pricing strategies.....	26
Figure 9: Normalised price change under net price transparency in selected European markets	27
Figure 10: Normalised price change under net price transparency within a group of countries such as the Valletta Declaration.....	28
Figure 11: Payers were undecided as to the impact of greater NPT on access but did not believe access would improve.....	39
Figure 12: Price convergence means that countries with more stringent budget constraints will be kept out of the market and see increased delays to access	40
Figure 13: Three products in three TAs were explored during the payer survey	41

Table of Tables

Table 1: Definition of ‘pricing transparency’ vs ‘price transparency’	vi
Table 2: European countries supporting and dissociated from the draft proposal of the resolution for greater public disclosure of prices and R&D costs (2019).....	4
Table 3: Approach to the structured literature review	6
Table 4: Individuals surveyed in the national payer survey	8
Table 5: European experts participating in the advisory board	8
Table 6: Definition of ‘pricing transparency’ vs ‘price transparency’	11
Table 7: Mechanisms used by national, regional and local health authorities to determine the price paid for a medicine	13
Table 8: Any proposal on transparency needs to specify type of information and to whom it is transparent and compliance with existing legal requirements	15
Table 9: Qualitative justification for supporting NPT based on the principle that ‘transparency = good’	17
Table 10: Current level of transparency for nationally agreed Net Prices in European markets represented in the advisory board.....	18
Table 11: Overall perceptions of the impact of negotiating confidential discounts on patented pharmaceuticals in 10 public and statutory health systems surveyed (n = 10)	22
Table 12: Qualitative justification for supporting NPT based on increased information available for negotiation.....	23
Table 13: Qualitative justification for opposing greater NPT based on expected changes in industry strategy	23
Table 14: Payers highlighted that the impact of greater NPT will depend on current net prices, which are confidential.....	24
Table 15: Expected effect of greater NPT on the use of common pricing mechanisms	31
Table 16: The implications of disclosing R&D costs	45

1. Introduction

As a response to the intense international debate on the transparency of biopharmaceuticals prices in Europe, Merck Sharp & Dohme (MSD) asked Charles River Associates (CRA) to curate a panel of experts to develop evidence on the impact of greater net price transparency (NPT) of innovative medicines. Professor Walter Van Dyck²³ and Professor Massimo Riccaboni²⁴ were asked by CRA to lead the research into the impact of greater NPT, supported by a wider panel of 10 experts from a range of European markets. This white paper documents the results of this analysis: first, defining the concept of NPT, then integrating the perspective of a diverse pool of expert stakeholders, and finally validating the findings through the development of a computational model of the consequences for European stakeholders of an increased level of transparency of NPT.

1.1. Background of the debate

The merits of having more or less transparency on prices has been a topic for discussion not just in the life science sector but across businesses and industry in general for many decades. On one hand, classical economic theory posits “perfect competition” (an idealistic scenario) where purchasers have full information on prices and product characteristics, and this results in a market outcome with uniform and competitive prices for comparable goods to the benefit of society.²⁵ On the other hand, there are theoretical arguments against price transparency. Firstly, given the realities of how markets work, economic theory shows that in more concentrated markets or markets where goods are imperfect substitutes (as could be argued in the case of innovative pharmaceuticals), information exchanges and increased price transparency can have anticompetitive effects, leading to higher prices and a lower output, to the detriment of society.²⁶ In particular, the reduction of the uncertainty in competitive price negotiations (i.e. reduction of the need to offer a better discount relative to the competitor) and the introduction of effective means to support tacit collusive agreements (i.e. competitors will know if net prices do not follow specific patterns) can further diminish competition.^{27,28} Secondly, establishing different prices across different markets can lead to a higher level of output (or access when considering pharmaceuticals) and incentivise innovation – price transparency can thus be determined detrimental to innovation if it leads to price convergence.²⁹ It is also important to note that beyond a purely economic assessment, based on

23 Associate Professor of Technology & Innovation Management, Vlerick Business School, Belgium

24 Professor of Economics, AXES Research Unit at IMT School for Advanced Studies, Lucca, Italy

25 Kaya, A., & Liu, Q. (2015). “Transparency and price formation.” *Theoretical Economics*, 10(2): 341–383.

26 Boone, J., & Pottersz, J. (2006). “Transparency and prices with imperfect substitutes.” *Economics Letters*, 93(3): 398–404.

27 Kyle, M.K. & Ridley, D.B. (2007). “Would Greater Transparency and Uniformity of Health Care prices Benefit Poor Patients?”. *Health Affairs*, 26 (5): 1384–1391. DOI 10.1377/hlthaff.26.5.1384

28 Danzon, P. M., & Towse, A. (2003). “Differential pricing for pharmaceuticals: reconciling access, R&D and patents.” *International journal of health care finance and economics*, 3(3): 183–205.

29 Berdud, M., Chalkidou, K., Dean, E., Ferraro, J., Garrison, L., Nemzoff, C., Towse, A. (2019). The Future of Global Health Procurement: Issues around Pricing Transparency. Research Paper 19/04, Office of Health Economics

efficiency and utility, there are other arguments for transparency associated with good governance and enhanced democracy.

The debate on transparency in the purchase of pharmaceuticals is also long-standing. For example, in the European Union (EU), the 'Transparency Directive' (Council Directive 89/105/EEC)³⁰ defines a series of procedural requirements designed to verify that national pricing and reimbursement decisions do not create obstacles to the pharmaceutical trade within the EU's Internal Market.

However, the international debate on net price transparency of innovative medicines has intensified in recent years. While it is generally understood that confidential pricing agreements have been introduced to reduce the impact of medicines cost on the budget and to improve the use of new technologies, there have also been claims that the existence of confidentiality agreements has meant that the list prices are not the actual prices of medicines, impacting those countries that use list prices in other markets as part of their price determination process.³¹ In the past few years, in addition to advocacy groups, organisations such as the United Nations (UN), the World Health Organization (WHO) and the Organisation for Economic Co-operation and Development (OECD)³² have published reports calling for an international focus on transparency in the pharmaceutical sector and focused specifically on prices. This culminated with the World Health Assembly (WHA) approving a resolution to support greater public disclosure of prices and research and development (R&D) costs for medicines and other health products. This was approved in May 2019 with support from governments in 22 other countries, including several European markets.³³ In addition, in September 2020, the WHO published a new pricing policy guideline³⁴ recommending that countries improve the transparency of pricing processes and prices.

Focusing on European countries, it is not uncommon for European payers to request pharmaceuticals to disclose the confidential net prices negotiated with other countries to inform their own pricing process either through formal (for example in Austria where statutory discounts in referenced member states should be '*taken into account*'³⁵) or informal (for example in the Netherlands when the minister of health wrote an open letter to pharmaceutical companies to request

30 EUR-Lex : Access to European Union Law [las accessed 14 December 2020]: <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A31989L0105>

31 Iunes, R.F., Uribe, M.V., Torres, J.B. et al. (2019). "Confidentiality agreements: a challenge in market regulation". *Int J Equity Health* 18, 11 <https://doi.org/10.1186/s12939-019-0916-3>

32 OECD (2017). "New Health Technologies, Managing Access, Value and Sustainability". Available at <https://images.politico.eu/wp-content/uploads/2017/01/OECD-on-new-drugs-and-pricing.pdf>

33 The Seventy-Second World Health Assembly, Agenda item 11.7 (2019). "Improving the transparency of markets for medicines, vaccines, and other health products". Available at http://www.salute.gov.it/imgs/C_17_notizie_3769_listaFile_itemName_0_file.pdf

34 WHO (2020). "WHO guideline on country pharmaceutical pricing policies". Available at <https://apps.who.int/iris/bitstream/handle/10665/335692/9789240011878-eng.pdf>

35 Bundesministerium für Gesundheit und Frauen (2017). Regelung für die Vorgehensweise der Preiskommission bei der Ermittlung des EU-Durchschnittspreises gemäß § 351c Abs. 6 ASVG. Available at <https://www.sozialministerium.at/Themen/Gesundheit/Medizin-und-Gesundheitsberufe/Medizin/Arzneimittel/Arzneimittelpreise/EU-Durchschnittspreise-laut-ASVG.html>

greater price transparency³⁶) channels. More recently, following the resolution approved by the WHA, a Decree has been published in Italy stating that the manufacturer must provide information about “marketing, consumption and the reimbursement in other countries ... including any further negotiation agreements” in order to begin the reimbursement negotiation process.³⁷ However, it is important to note that confidential agreements made in other markets have been respected by the implementation guidelines published in September.³⁸ Beyond payers and policymakers, new stakeholders are focusing on NPT: for example, in France, a new civil group called the ‘Drug Transparency Observatory’ has been launched to “closely monitor” government implementation of the WHA resolution.³⁹

There are clearly very different views on the merits of NPT. The purpose of this analysis is to understand these different perspectives and look for consensus. It is therefore useful to start with the published views of different stakeholders.

1.2. Views of key stakeholders: policymakers, NGOs and the industry

The views of the policymakers

One way to look at the view of European policymakers is to consider support for the recent proposal that was submitted to the WHA in 2019, led by the Italian Ministry of Health.⁴⁰ The proposal was supported by 22 countries (including 9 European countries); however, 3 European markets have actively dissociated themselves from the final document, arguing that there has been insufficient time to evaluate the complex implications of such a resolution (Table 2).⁴¹ The final vote resulted in the adoption of the proposal, with a large number of countries voting for its approval, showing that at a policymaker level there is considerable, although not universal, support for transparency.

36 Medicines Law and Policy (2019). “Dutch Minister of Health writes open letter to pharma, threatens to name and shame”. Available at <https://medicineslawandpolicy.org/2019/08/dutch-minister-of-health-writes-open-letter-to-pharma-threatens-to-name-and-shame/>

37 AIFA (2020). “Decreto 10 Luglio 2020”. Available at <https://www.gazzettaufficiale.it/eli/gu/2020/07/24/185/sg/pdf>

38 AIFA (2020). “Linee guida per la compilazione del Dossier a supporto della domanda di rimborsabilità e prezzo di un medicinale”. Available at: https://www.aifa.gov.it/documents/20142/0/AIFA_Linee+Guida_v.+16.9.2020+per+consultazione+pubblica.pdf/64f8d5b5-69df-a799-9ae7-36a5743d5f17

39 Health Policy Watch, medicines & Vaccines (2019) “New Drug Transparency Observatory Launched In France”. Available at <https://healthpolicy-watch.news/new-drug-transparency-observatory-launched-in-france/>

40 The Seventy-Second World Health Assembly, Agenda item 11.7 (2019). “Improving the transparency of markets for medicines, vaccines, and other health products”. Available at http://www.salute.gov.it/imgs/C_17_notizie_3769_listaFile_itemName_0_file.pdf

41 WHO (2019). “World Health Assembly Update, 28 May 2019”. Available at <https://www.who.int/news-room/detail/28-05-2019-world-health-update-28-may-2019>

Table 2: European countries supporting and dissociated from the draft proposal of the resolution for greater public disclosure of prices and R&D costs (2019)

In support of the draft resolution	Actively dissociated from the draft resolution
Andorra	Germany
Italy	Hungary
Luxembourg	United Kingdom
Malta	
Portugal	
Russia	
Serbia	
Slovenia	
Spain	

Source: Pharma World Magazine (2019). “The WHA has approved the resolution of transparency of drug prices”. Available at <https://www.pharmaworldmagazine.com/the-wha-has-approved-the-resolution-on-transparency-of-drug-prices/> ; WHO (2019). “Improving the transparency of markets for medicines, vaccines, and other health products”. Available at http://www.salute.gov.it/imgs/C_17_notizie_3769_listaFile_itemName_0_file.pdf

Note: The final proposal was adopted with the majority of the votes of the WHA; however, the votes of individual countries are unknown.

The views of NGOs

The view of non-governmental organisations (NGOs) has typically been to support greater NPT, especially with regard to improving access to medicines in lower-income countries. For instance, Médecins Sans Frontières published an article in 2019 titled ‘*Secret Medicine Prices Cost Lives*’. This article was published in advance of the 2019 WHO Fair Pricing Forum in which increased transparency in medicines pricing was a key topic for discussion. The article states: ‘*Fair pricing depends on fair negotiations, and there cannot be fair negotiations without transparency*’. The same article also states that confidentiality prevents there being a direct connection between R&D costs and medicine prices, indicating that a key rationale for supporting price transparency comes from the hope of moving towards a cost-plus pricing model.⁴²

In recent years, new NGOs within Europe have also supported increased price transparency. For instance, as mentioned, the ‘Drug Transparency Observatory’ has formed in France following the adoption of the WHA resolution. The Observatory calls on the French government and all countries to implement not only the adopted resolution on the transparency of medicines markets but also the transparency measures included in the initial resolution draft, which go beyond just medicines pricing.⁴³

⁴² Médecins Sans Frontières (2019). “Secret medicine prices cost lives”. Available at <https://msfaccess.org/secret-medicine-prices-cost-lives>

⁴³ Health Policy Watch (2019). “New Drug Transparency Observatory Launched in France. Available at <https://dontradeourlivesaway.wordpress.com/2019/06/17/new-drug-transparency-observatory-launched-in-france/>

On the other hand, some NGOs have recognised the value of confidential agreements to provide efficient access to medicines and ensure the sustainability of the national health system. For example, in Italy, Cittadinanzattiva (a consumer organisation) and the CnAMC⁴⁴ responded to recent draft guidelines published by the Italian Medicines Agency (AIFA) stating that “*violating the confidentiality clauses would mean questioning the agreements and inevitably lengthen access times (if not prevent) for some highly innovative therapies*” and that “*this could also affect the sustainability of the healthcare system [expenditure]*”.⁴⁵ Their position was also supported by 32 Italian patient organisations.

The views of the biopharmaceutical industry

Although the innovative biopharmaceutical industry is accused of being against transparency, it has supported several initiatives to increase transparency across various domains of the pharmaceutical sector. For example, the industry has worked with the European Commission and national governments on the improved transparency of clinical trial information and information regarding the relationship with healthcare professionals.⁴⁶ However, with regard to NPT, the view of the biopharmaceutical industry remains that NPT would, given the use of international reference pricing, lead to price convergence and reduced access to patients.⁴⁷ Indeed, in a response to an EC draft opinion on innovative payment models for high-cost innovative medicines, the European Federation of Pharmaceutical Industries and Associations (EFPIA) makes its position on the value of confidential price agreements clear, stating: “*Confidentiality of net prices creates incentives for innovation while facilitating access to medicines for countries with lower ability to pay.*”^{48,49}

44 Coordinamento nazionale delle Associazioni dei Malati Cronici which translates to “National Coordination of Associations of Chronic Patients”. The CnAMC is a Cittadinanzattiva network which represents an alliance between associations and federations of people affected by chronic and rare diseases.

45 Cittadinanzattiva (2020). “Consultazione pubblica sulle ‘Linee guida per la domanda di rimborsabilità e prezzo di un medicinale’, pubblicate dall’Agenzia Italiana del Farmaco il 16 settembre 2020”. Available at <https://www.parkinson-italia.it/wp-content/uploads/2020/10/CITTADINANZATTIVA-Consultazione-pubblica-linee-guida-domanda-rimborsabilita-prezzo-di-un-medicinale.pdf>

46 Baronikova, S., Purvis, J., Southam, E., Beeso, J., Panayi, A., & Winchester, C. (2019). “Commitments by the biopharmaceutical industry to clinical trial transparency: the evolving environment.” *BMJ evidence-based medicine*, 24(5): 177–184.

47 MAP BioPharma (2019). “Pricing transparency proposals challenged by EFPIA”. Available at <https://mapbiopharma.com/home/2019/08/pricing-transparency-proposals-challenged-by-efpia/>

48 EFPIA (2017). “EFPIA Response to Draft Opinion on Innovative payment models for high-cost innovative medicines”, https://www.efpia.eu/media/288630/final_efpia-response-to-exph-draft-opinion-7_12_2017_wir.pdf

49 Roediger, A. (2019). “Blinded by the light: A first step towards trust could be a transparent conversation about the principles we as stakeholders have in common. The EFPIA Oncology Platform sees itself as an attempt to do so. One such principle is certain: that there is no valuable innovation without a patient who can access and benefit from it”. Available at <https://www.efpia.eu/news-events/the-efpia-view/blog-articles/blinded-by-the-light-quest-blog/>

1.3. A multifaceted methodology

As a response to the intense international debate on the transparency of medicine prices in Europe, the objective of this white paper has been to explore the technical aspects of the debate around greater NPT to add to the existing evidence focused more on high-level principles. A multifaceted approach has been taken to realise this goal:

- A structured literature review
- A qualitative survey of a sample of European payers on the benefits and costs of NPT
- The establishment and consultation of an expert advisory board representing a range of different European countries
- Development of a computational model analysis of the impact of NPT on European countries

The development of the computational model has been led by Professor Van Dyck and Professor Riccaboni. Ultimately the objective is to publish the results of the computational model in a peer-reviewed journal separate to this white paper. This white paper provides an interim analysis summarising the consensus reached during an advisory board with the co-authors of this publication. The coordination of the work and development of the paper has been facilitated by CRA, and sponsored by MSD, but the intellectual contribution is attributable to the experts authoring this analysis.

The structured literature review

The literature review followed a tiered approach. We first reviewed papers setting out the economic theory both for and against greater NPT in the innovative pharmaceutical industry, including the theoretical consequences of greater NPT. Paper were selected according to their technical robustness and relevance to the topic (Table 3).

Table 3: Approach to the structured literature review

Topic	Description
Key words	“pharmaceutical prices”; “transparency”; “confidentiality” “rebates disclosure” and permutations (e.g. <i>price</i> instead of <i>prices</i>)
Search engines	Google Scholar; Google; EconLit; PubMed
Date range	Consideration of recent studies published since 2010
Search language	English
Reviewing process	Two reviewers researching the literature independently and consolidating their findings

Selection process	Relevant papers have first been scrutinised based on the relevance of their titles and abstracts. Relevant articles have been read in full, and only articles with robust economic and technical approaches have been considered
Handsearch	Inclusion of additional relevant studies referenced in the papers initially selected (relevant non-English studies have been identified and included through handsearch)

Source: CRA

In total, 22 studies were identified and reviewed. These studies have been used to distil a list of potential implications (both positive and negative) from greater NPT that were summarised as background to the advisory board meeting. The findings from the review summarised the full range of potential consequences, with both the potential advantages and disadvantages presented to experts during one-to-one interviews prior to the advisory board.

A more detailed literature review was then undertaken to identify econometric or simulation analysis testing the impact of increased NPT for the prices of branded, on-patent medicines on the budget of national payers in Europe. As confirmed by the recent systematic literature review conducted by the WHO,⁵⁰ there are no studies available to document this.

Finally, we looked beyond the literature on innovative medicines, to identify different approaches to building a computational model: these articles look at the technical aspect of different modelling approaches. The main objective of the review was not to systematically review all the publications in the field but to collect the building blocks of the model presented in this analysis.

A survey of the current view of European payers with respect to NPT

While the perspectives of policymakers/politicians, academics and NGOs are well known and usually receive wide media coverage, the perspectives of national payers are often less known. To gather a snapshot of the views of different payers within Europe, we conducted an online survey of 16 European payers representing 10 European countries (Table 4). Individuals interviewed represented a range of payer decision makers or payer advisors from key national pricing bodies. The countries were selected to ensure that a range of different European geographies and country characteristics were represented in the results (both larger and smaller countries, different levels of income and different regions: Nordics as well as Southern, Western and Eastern European). The objective was to survey two payers per country, although in some circumstances this was not possible.⁵¹ The survey was conducted online through SurveyMonkey in July 2020.

50 WHO (2020). "WHO guideline on country pharmaceutical pricing policies". Available at <https://apps.who.int/iris/bitstream/handle/10665/335692/9789240011878-eng.pdf>

51 In one case, the payer surveyed is also a member of the advisory board. In the cases of Greece, Poland, Portugal and Sweden, only one payer/payer advisor was surveyed from each.

Table 4: Individuals surveyed in the national payer survey

Country	#	Organisation	Role of individual 1	Role of individual 2
France	2	CEPS	Ex-payer	Ex-payer
Germany	2	G-BA	Ex-payer	Payer advisor
Greece	1	EOPYY	Ex-payer	–
Italy	2	CPR (AIFA)	Ex-payer	Current payer
Netherlands	2	ZIN	Payer advisor	Payer advisor
Poland	1	MoH	Ex-payer	–
Portugal	1	INFARMED	Payer advisor	–
Spain	2	DGFPS	Ex-payer	Ex-payer advisor
Sweden	1	TLV	Ex-payer	–
England	2	NICE	Current payer	Ex-payer advisor

Source: CRA

The survey included questions on the payer’s preference for greater NPT, the type of information they would like to be disclosed and they would be ready to disclose, their expectation in terms of impact of increased transparency on prices and access, and how these would vary across different therapy areas and scenarios for information disclosure.⁵² Responses were anonymised as per European General Data Protection Regulation (GDPR) requirements, and some key insights were used as input to the advisory board discussion.

The establishment and consultation of an expert advisory board

To try to develop a consensus on the economic impact of NPT in Europe, building on the results of the payer survey, an expert advisory board of economic and health economic experts from 12 European markets was established. The selection of the experts was made following two criteria: First, 12 European countries were identified to be representative of the different national contexts that can be observed across Europe (considering market size and relative income of the markets). Second, for each of the markets, an economic or health economic expert was identified based on their expertise on NPT (based on publications and participation in national debates). The final list of experts involved in the advisory board is shown in alphabetical order of their respective countries (Table 5).

Table 5: European experts participating in the advisory board

Country	Expert
 Belgium	Walter Van Dyck *, <i>Vlerick Business School</i>
 Croatia	Luka Voncina, <i>University of Rijeka</i>
 France	Pierre Bentata, <i>Asterès and Y Schools</i>

52 Survey questions can be provided upon request.

 Germany	Wolfgang Greiner, <i>Bielefeld University</i>
 Greece	Kostas Athanasakis, <i>National School of Public Health</i>
 Italy	Massimo Riccaboni *, <i>IMT School for Advanced Studies</i>
 Netherlands	Wim Groot, <i>Maastricht University</i>
 Poland	Marcin Czech, <i>Warsaw University of Technology</i>
 Portugal	João Marques-Gomes, <i>Nova University Lisbon</i>
 Spain	Jorge Mestre-Ferrandiz, <i>Universidad Carlos III Madrid</i>
 Switzerland	Pius Gyger, <i>Independent Consultant, previously member of Federal Commission of Drugs (EKDF)</i>
 UK	Jack Scannell, <i>Innogen Institute, Innogen Associate, University of Edinburgh</i>

*Leading investigators

Each expert was interviewed individually prior to the collective discussion to collect their views on the topic of NPT,⁵³ their understanding of the consequences of increased NPT (especially in reference to their respective countries) and the economic arguments and evidence to support their views. The findings from the individual interviews were consolidated as background to the advisory board, identifying areas of consensus but also of divergent opinions, and presented to an advisory board meeting involving all the experts. The meeting took place virtually on 26 August 2020. All the experts on the board were invited to provide their opinions on the different topics under Chatham House rules.⁵⁴ Comments from the participants were provided verbally but also discussed in the virtual chat of the meeting platform. In the meeting, we discussed whether there was consensus about the consequences of greater NPT on national budgets, on financial incentives for the industry and future R&D, and on patient outcomes and access to treatment. This was subsequently written up, and the same experts were given the opportunity to review the record of the advisory board. The results from the discussion are presented in this white paper.

53 Due to availability, the initial one-to-one call with the French experts was attended by a team of economists from the same firm (*Asterès*): Professor Nicolas Bouzou, Charles-Antoine Schwerer and Alice Bouleau

54 The principle that information disclosed during the meeting may be reported by those present, but the source of that information may not be explicitly or implicitly identified.

Results from a computational model⁵⁵

As noted in the literature review, most of the papers on NPT are theoretical in nature, and with little empirical evidence being presented to show the expected impact of greater NPT in Europe. Experts highlighted that this is because greater NPT remains a theoretical change and we do not have transparent prices implemented in the vast majority of the countries at present. To address this gap in the literature, a computational model has been developed by the two leading investigators (Professor Walter Van Dyck and Professor Massimo Riccaboni). This computational model explores the effects of Europe-wide NPT policy on the net pharmaceutical prices reached in different countries. The model works by simulating the country-level bargaining process that takes place between a country's payer authority and the manufacturer and by considering what would happen if there was NPT. In this case, the price reached in each of the countries considered would be made visible for reference in all other countries. The full methodology and results of this computational model are presented in a separate technical research paper; in this white paper we include the main findings.

1.4. Structure of the white paper

This white paper presents the views expressed by economic and health economic experts during an advisory board meeting and discusses the degree to which there is a consensus across experts. Additional evidence from the payer survey and the structured literature review are integrated into the analysis throughout the white paper, and key insights from the computational model developed in tandem have been summarised in Section 3.1. In Chapter 2, we define the concept of NPT. In Chapter 3, we analyse the consequences of greater NPT on national budgets. Chapter 4 discusses the impact of increased NPT on the functioning of the pharmaceutical market. In Chapter 5 we look at the impact NPT has on patients, and whether this varies in terms of disease area. Chapter 6 presents our conclusions on the implications of increased NPT.

55 Van Dyck, W., Riccaboni, M., & Swoboda, T. 2020. Pharmaceutical net price transparency across European markets: Insights from a Multi-Agent simulation model, Vlerick Policy Paper Series #13. Brussels, Belgium: Healthcare Management Centre, Vlerick Business School.

2. Putting the net price transparency debate into context

KEY FINDINGS

- Requests for ‘greater transparency’ are often made without recognising the difference between ‘price transparency’ and ‘pricing transparency’; there is therefore a need to understand this distinction and to provide clarity on the definition of ‘net price transparency’ as in the scope of this white paper.
- The practical challenges of making net price information transparent in a meaningful way are often overlooked:
 - How to account for the multiple net prices that one medicine can have in a market
 - How to account for situations in which the price is calculated through a managed entry agreement (MEA) or retrospectively
 - How to account for current confidentiality clauses in national legislation

2.1. A definition of ‘net price transparency’

To advance the debate on transparency, it is important to make a distinction between requests for the disclosure of confidential information and requests for increased transparency in decision-making (Table 6). Often these two requests are not separated by advocates, with many requests made more generally for ‘greater transparency’ or with definitions conflating both pricing (i.e. pricing process) and price transparency.

Table 6: Definition of ‘pricing transparency’ vs ‘price transparency’

<u>Pricing</u> transparency <i>Or pricing process transparency</i>	Transparency of the process used to determine prices, aiming to ensure accountability of the reimbursement decision-making process
<u>Price</u> transparency	Transparency of the final price level agreed between payers and manufacturers, aiming to disclose any preferential rebates a payer may have achieved

Source: CRA

Our paper focuses on transparency of net prices (price transparency) and the ongoing debate regarding the potential economic consequences of such a measure. The beneficial role of transparency in the decision-making process (pricing transparency/pricing process transparency) is generally agreed across payers and industry (although many markets do not employ such transparent measures) and is associated in the literature with good governance, enhanced democracy and efficiency. Transparency of governance and decision-making, particularly regarding purchasing decisions, helps to build trust amongst the public (when it is taxpayer money being used) but also amongst competitors and those responsible for ensuring markets work effectively, i.e.

regulators. With regard to medicines, and their prices in particular, a range of stakeholders support transparency of the price negotiation process in order to better understand whether the price has been negotiated following a given set of rules established to protect the interests of all the stakeholders, and to ensure the accountability of the pricing and reimbursement decision-making process.⁵⁶ Some experts have suggested that instead of looking for greater price transparency, markets which do not have effective pricing transparency measures should focus on this to ensure that they are not overpaying for medicines from a local value perspective.⁵⁷

This is different to the debate on NPT, which refers to the concept that the ex-factory price of a medicine, as agreed through confidential pricing mechanisms between national payers and manufacturers, is made transparent to third parties.

We note that there are many different prices associated to medicines: there is the list price publicly disclosed by the manufacturer, the price including distribution margins and taxes, the prices agreed with the national payer after taking into account rebates, discount and clawbacks. The price can also vary depending on whether the product goes through a regional process or is subsequently negotiated at the hospital level. However, in line with the ongoing debate, we define NPT as referring to the price agreed with the national payer to be paid to the manufacturer of a product after taking into account rebates, discounts, clawbacks and managed entry agreements.⁵⁸

2.2. The practical challenges associated to ‘net price transparency’

Although the marketing authorisation process for medical products is harmonised for EU Member States (through the European Medicines Agency), pricing and reimbursement remains a national competence, meaning that a national price for a medicine is normally agreed between the manufacturer and the relevant national authority (the payer).⁵⁹ There is often a published price – this is commonly defined as the “list” price. However, this is rarely the price actually paid for a medicine or the amount of money that the manufacturer receives. This is due to confidential negotiations between said national payer and the manufacturer. Further to this, the final price of an innovative medicine can be further impacted by additional sub-national pricing agreements with regional authorities, further discounts agreed with hospitals or groups and margins implemented by wholesalers (Table 7). It is also possible for broader caps by therapy area or on branded pharmaceuticals in general to be applied at the national level to cap expenditure. The result is that

56 Roediger, A. (2019). “Blinded by the light: A first step towards trust could be a transparent conversation about the principles we as stakeholders have in common. The EFPIA Oncology Platform sees itself as an attempt to do so. One such principle is certain: that there is no valuable innovation without a patient who can access and benefit from it”. Available at <https://www.efpia.eu/news-events/the-efpia-view/blog-articles/blinded-by-the-light-guest-blog/>

57 CRA Expert Advisory Board

58 This does not consider additional discounts made at the sub-national level because the main request from advocates of greater NPT appears to be around the national net prices (moreover, on a technical ground, while there are already considerable differences between the structures of European national healthcare systems, which make cross-country comparisons relatively uninformative, differences at sub-national level are even more pronounced).

59 WHO (2020). “Medicines Reimbursement Policies in Europe”. Available at https://www.euro.who.int/data/assets/pdf_file/0011/376625/pharmaceutical-reimbursement-eng.pdf

there are many different net prices associated with a single innovative medicine, indicating a key practical challenge with implementing greater NPT.

Even at the national level it can be hard to define the ‘net price’ of a medicine, due to the implementation of payment mechanisms such as MEAs. MEAs are arrangements between manufacturers and payers that are used to manage uncertainty and include terms conditional on how the medicine is used in practice. They generally take two forms: (1) performance-based agreements that link the price or rebate level to the performance of a medicine (this can be established upon the collection of real-world data over a number of years) or (2) financial-based agreements that link the price or rebate level to metrics such as the volume of product used or cost-savings made as a result of product use.⁶⁰ As a result of MEAs, the national “net price” of a medicine is often not known to either the ‘buyer’ or the ‘seller’ until after a given period, when either outcomes are known or usage metrics have been collected.

Table 7: Mechanisms used by national, regional and local health authorities to determine the price paid for a medicine

	Description
Managed entry agreement (MEA)	A contractual agreement that enables reimbursement of a medicine subject to specified conditions. Conditions can be finance-based (e.g. cost caps, volume discounts) or performance-based (e.g. dependent on further evidence development, dependent on outcomes). ⁶¹
Sub-national negotiation	In many markets, regional bodies determine reimbursement and can negotiate further discounts on a nationally agreed Net Price, either through the implementation of MEAs (see above) or through simple discounts and negotiations (e.g. with 17 regions in Spain ⁶²). Further to this, if a product does not receive national reimbursement, there are mechanisms for a manufacturer to gain access through individual negotiations with regional authorities (e.g. with clinical commissioning groups (CCGs) in the UK ⁶³)

60 OECD (2019). “Health Working Paper No. 115: Performance-based managed entry agreement for new medicines in OECD countries and EU member states”. Available at <https://www.oecd.org/health/health-systems/HWP-115-MEAs.pdf>

61 WHO (2020). “Medicines Reimbursement Policies in Europe”. Available at <https://www.euro.who.int/en/publications/abstracts/medicines-reimbursement-policies-in-europe>

62 ISPOR (2020). “Global Health Systems Road Maps – Pharmaceutical HTA and Reimbursement Processes – Spain”. Available at https://tools.ispor.org/htaro_admaps/Spain.asp

63 Monitor (2013). “Local price setting and contracting practices for NHS services without a nationally mandated price: A research paper”. Available at <https://www.gov.uk/government/publications/local-price-setting-and-contracting-for-nhs-services-without-a-national-price>

Hospital negotiations	<p>Across Europe, hospitals tend to have autonomy on formulary and procurement decisions as well as additional restrictions on use (in some markets certain inpatient medicines are centrally procured). Part of gaining hospital formulary access can include additional discounts on prices.</p> <p>In many European markets (e.g. Romania, Czechia, Denmark) tendering is common for most inpatient medicines and is the responsibility of the hospitals.⁶⁴</p>
Wholesaler margins	<p>Most countries have a mixture of national and regional wholesalers supplying medicines to pharmacies. These can be private or public (public being Central Medical Stores). Wholesalers purchase medicines at the “Net Price”, or Manufacturer Selling Price (MSP), but are able to make a margin on this when selling to retailers/health facilities.⁶⁵</p>

The second complexity regarding NPT is transparency to whom. Requests for greater NPT should clarify exactly what is being requested to be made transparent (e.g. final price level, specific terms of agreements, discounts at the regional level, etc.) and also to whom the information should be disclosed (e.g. national pricing authorities, the public, other manufacturers, governments, other non-European markets, etc.). In some cases, transparency can be requested from a country’s own pricing authority (i.e. intra-country transparency). For example, in some countries (e.g. Belgium), governments do not have transparency on the price agreed by their own payers and are therefore looking for more transparency within their own country. Alternatively, it could be transparency intended for patients/the general public in a country. However, the debate tends to focus on greater NPT across countries, with requests from one country to know the price being paid in another country (i.e. inter-country transparency). This is the case with the recent WHA resolution, led by the Italian government and supported by many other national governments, which is asking for national net prices across Europe to be made public by the manufacturers for the purposes of negotiation. Experts highlighted that it is critical that advocates for greater NPT are clearer about the form of NPT they are requesting in order for the subsequent debate to be sufficiently informed and dealing with less uncertainty.

Finally, when considering how legislation for greater NPT would be implemented, it is necessary to consider the legal measures in place that currently maintain NPT for innovative medicines and therefore how new legislation (made at a national or international level) would dovetail with this. Currently, negotiations between payers and manufacturers result in agreements that often include requirements on confidentiality (often requested by both parties) that are mandated at a national level (for example Patient Access Schemes used in the UK ⁶⁶). If greater NPT were to be

64 Vogler, S., Zimmermann, N., Leopold, C., Habl, C., & Mazag, J. (2013). “Discounts and Rebates Granted for Medicines for Hospital Use in Five European Countries”. *The Open Pharmacoeconomics & Health Economics Journal*, 5(1). DOI: 10.2174/1876824520130426001

65 WHO (2008). “Measuring medicine prices, availability, affordability and price components”. Available at: https://www.who.int/medicines/areas/access/OMS_Medicine_prices.pdf

66 Jaroslowski S, Toumi M. Design of patient access schemes in the UK: influence of health technology assessment by the National Institute for Health and Clinical Excellence. *Appl Health Econ Health Policy*. 2011 Jul 1;9(4):209-15. doi: 10.2165/11592960-000000000-00000. PMID: 21682349.

implemented either at the national or international level without explicitly stating how current confidentiality clauses should be taken into consideration, new legislation would likely be in breach of current pricing contracts, putting industry in an extremely complicated position. Country affiliates within an international company would not be able to share pricing information from other markets with their own payer authority despite requests.

In conclusion, any proposal to increase NPT should be carefully articulated and consider all the technical aspects; otherwise it would be difficult to initiate a productive debate on the merits and consequences of such a proposal (Table 8).

Table 8: Any proposal on transparency needs to specify type of information and to whom it is transparent and compliance with existing legal requirements

	Description
What information is made transparent?	There are several components to a Net Price agreement further to the price alone (e.g. specific repayment terms, renegotiation periods). In addition, there is contextual information (e.g. the rationale used to obtain a net price discount).
Who is the information made transparent to?	Is this intra-country transparency or inter-country transparency, and which stakeholders is the information being made available to?
Can the information be made transparent?	Confidential agreements are common across European countries. ⁶⁷ Proposals regarding greater NPT need to explain implications for the legal frameworks that are already in place.

⁶⁷ WHO (2020). "Medicines Reimbursement Policies in Europe". Available at https://www.euro.who.int/data/assets/pdf_file/0011/376625/pharmaceutical-reimbursement-eng.pdf

3. The political view is not always fully aligned with payers regarding the consequences of NPT on national budgets

KEY FINDINGS

- **Generally, all policymakers and payers support greater “transparency” in policy debates due to the associated positive connotations with this term.**
- **However, payers recognise that implementing greater NPT specifically, will have unintended consequences on national budgets and do not support its application in their own countries.**
- **There is a consensus that greater NPT is expected to result in price convergence across European markets but that this is unlikely to affect European expenditure on innovative medicines.**
- **There will be winners and losers from price convergence.**

3.1. Differences in the political and payer views

The view of policymakers on greater NPT are public and widely reported by the media. Their support for the WHA resolution is one such example. The academic evidence on the views of policymakers shows there are clearly significant concerns about the price of innovative medicines and affordability in the healthcare system. Innovative medicine prices are widely perceived to be unaffordable, and policymakers question how they are justified.⁶⁸ This indicates that perhaps pricing transparency (instead of NPT) would be a more appropriate solution. Moreover, the level of trust in the pharmaceutical industry is low⁶⁹ and there is a lack of understanding amongst many people (including politicians) regarding the development process for pharmaceuticals, which could be responsible for concerns about excessive profitability.⁷⁰ Based on their general support for the WHA resolution, we could assume that policymakers expect NPT would lead to lower prices and improved access. The views of those responsible for negotiating prices on behalf of public health systems (payers) are less clear. Beyond the personal thought pieces through which a number of individual experts have expressed their views, there is relatively little evidence.

To understand the views of payers, we conducted a payer survey in which we asked a group of current and former payers and payer advisors about both their support for greater NPT and their expectations about the impact of greater NPT (as per the definition outlined in Table 6). This was presented to and discussed with the experts who participated in the advisory board.

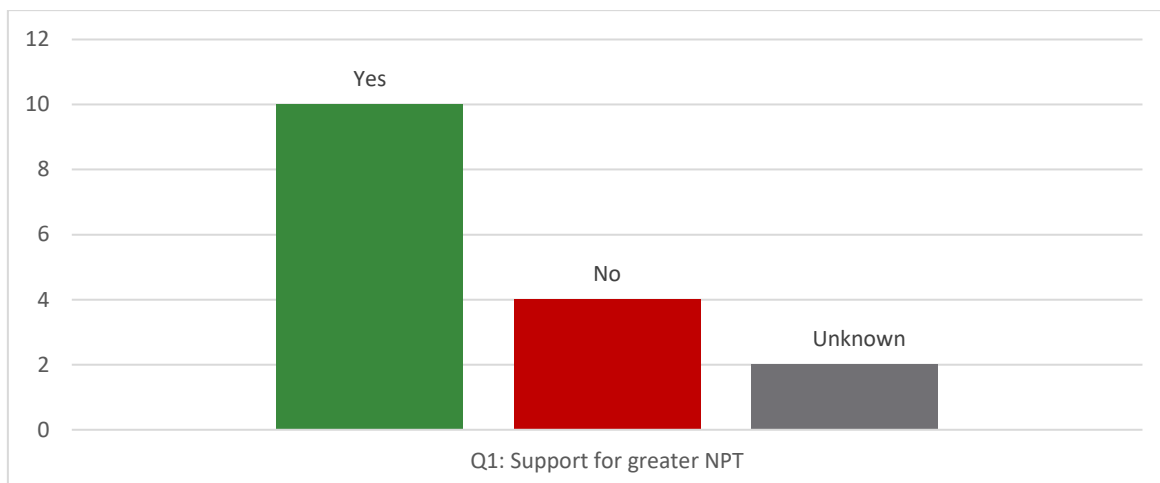
68 Zaprutko, T., et al. (2017). “Affordability of medicines in the European Union”. Available at <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0172753>

69 Edelman (2019). “2019 Edelman Trust Barometer, Trust in Healthcare”. Available at https://www.edelman.com/sites/g/files/aatuss191/files/2019-04/2019_Edelman_Trust_Barometer_Global_Health_Report.pdf

70 Heinemann, L. (2009). “Trust: Need for an Improved Communication between the Public World and the Pharmaceutical Companies”.

We first asked payers whether they support greater NPT and what net price information they would most like to have. In general, European payers declared they are in principle supportive of greater NPT (Figure 4).

Figure 4: Payers’ general support for greater NPT (n = 16)



Source: CRA Payer Survey (2020)⁷¹

We then asked payers what determined their views. Some payers justified their support for greater NPT on the basis that ‘transparency = good’ (Table 9). Given the structure of pricing policy in some European markets, the similarity between payers and policymakers may not be surprising. For example, in Poland the Minister of Health has final approval on all drug reimbursement, in Greece the payer authority has very little autonomy from the elected Ministry of Health and in Spain sub-national payer authorities are the elected local government officials.

Table 9: Qualitative justification for supporting NPT based on the principle that ‘transparency = good’

Market	Quote
France	<i>“When speaking about public money, a lack of transparency means a lack of democracy.”</i>
Portugal	<i>“I think that more transparency is better than less.”</i>
Spain	<i>“Taking into account that we are speaking about public money, there is no other option.”</i>

Source: CRA Payer Survey (2020).

71 CRA Payer Survey. Q1: “Do you support calls for greater Net Price Transparency (i.e. the disclosure of confidential prices agreed with manufacturers at the National level amongst European Markets, including your own)?”

There is also a question of equity. Currently, the level of NPT across European markets varies significantly, with only a few countries having some level of transparency (Table 10). Some respondents highlighted that this variation is not fair and that this should be addressed. One German payer commented that they “prefer harmonisation when it comes to this topic [net price transparency], but if other countries do not switch to net price transparency, Germany should depart from its present transparency,” and similarly a payer from Sweden stated, “Of course, the precondition is that many countries are involved in the process.”

Table 10: Current level of transparency for nationally agreed Net Prices in European markets represented in the advisory board

Country	Current level of national net price transparency	
Belgium	Confidential	Prices agreed at the national level are completely confidential and agreed through the process of negotiation.
Croatia	Confidential	Innovative medicines are priced confidentially and subject to budget caps (per therapy area (TA) or per product), and managed entry agreements are used.
France	Confidential	Prices agreed at the national level are completely confidential and agreed through the process of negotiation.
Germany	Partially transparent	Nationally agreed net prices are transparent through the Lauer-Tax to those with accounts, which requires a paid subscription. Further discounts/MEAs through sickness funds are possible and are not transparent.
Greece	Confidential	A series of confidential rebates are applied to official list prices. Recently, some products have been subject to formal, confidential negotiations.
Italy	Confidential	Discounts to nationally agreed prices are confidential. Frequent use of MEAs further reduces transparency.
Netherlands	Partially transparent	National prices are transparent, and, in most cases, no further discounts are made. Some ‘high priced products’ are subject to a further confidential discount at the national level.
Poland	Confidential	Implementation of MEAs and simple negotiated discounts mean net prices are kept confidential.
Portugal	Confidential	Prices agreed at the national level are completely confidential and are the result of a negotiation process.
Spain	Confidential	Prices agreed at the national level are completely confidential and agreed through the process of negotiation.

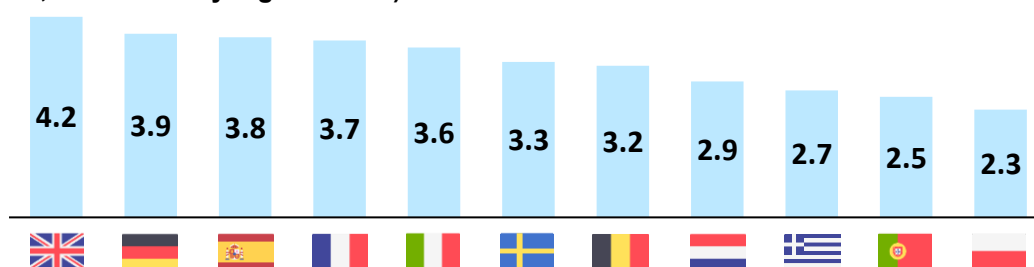
Switzerland	Partially Transparent	Ex-factory prices are listed transparently but represent the maximum price to be paid. A confidential rebate is often applied to this. Similarly, wholesale prices and prices paid by insurers/pharmacies are confidential.
UK	Confidential	Prices can be freely set at launch after marketing authorisation, although in many cases there is a PAS; ⁷² this involves a confidential discount, which is taken into account by the National Institute for Health and Care Excellence (NICE) when providing advice to NHS England.

Source: CRA Expert Advisory Board

Payers' preference for net price information in other markets

While one might expect payers to be most interested in net prices in lower-income markets (where medicine prices tend to be lower), the opposite was seen in the payer survey, with the highest levels of interest being shown in the net prices in relatively higher-income markets (e.g. Germany and the UK) and not those in lower-income markets (e.g. Greece and Poland) (Figure 5). Experts at the advisory board theorised that the high interest in UK prices was likely due to the fact that the UK health technology assessment (HTA) system is regarded as taking a strict approach to price determination (through their cost-effectiveness threshold), and payers would like to benefit from information about the resultant prices. It could be argued that this justifies improving the HTA systems in specific markets or sharing information on the value assessment process rather than asking for greater NPT.

Figure 5: Surveyed payers' level of interest in each European market's net price (1 = no interest; 5 = extremely high interest)



Source: CRA Payer Survey (2020)⁷³

One other interesting finding from Figure 5 is the high level of interest that payers expressed in the German net price, where pricing at the national level is already transparent.⁷⁴ The interest in German

⁷² PAS = Patient Access Scheme; often considered a form of financial Managed Entry Agreement (MEA)

⁷³ CRA Payer Survey: "Please indicate your level of interest for each of the following European markets, in having increased net price transparency".

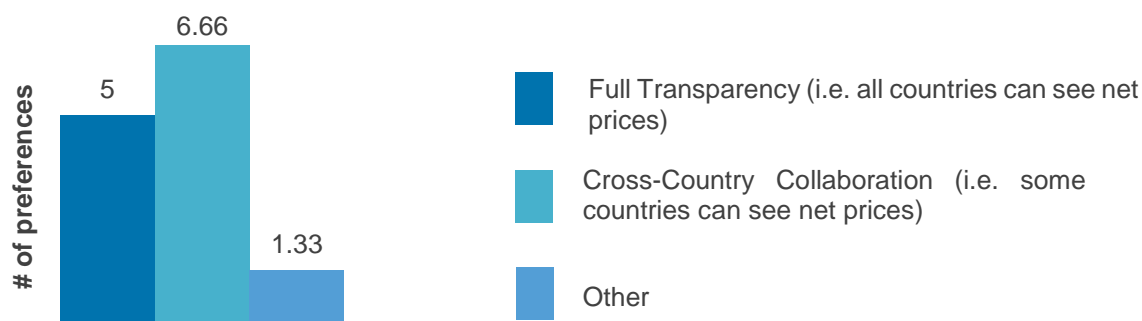
⁷⁴ Gandjour, A., Schüßler, S., Hammerschmidt, T., & Dintsios, C. M. (2020). "Predictors of negotiated prices for new drugs in Germany". *The European Journal of Health Economics*, 1–9.

prices shows the complexity in the current debate and perhaps the limited understanding of NPT today. Regarding the interest in both Germany and the UK, some experts also highlighted that the high level of interest in net prices in higher-income markets could be explained by curiosity about the ‘volume effect’ and whether larger, richer markets (with increased bargaining power) manage to achieve greater discounts based on the volume of a medicine they would be paying for.

In the UK, payers and politicians appear to be very much aligned in their attitude towards greater NPT. During the survey, UK payers consistently did not support greater NPT, based primarily on satisfaction with their own price-setting processes. Both UK payers highlighted that *“the UK works independently and has a strong HTA body (NICE) that evaluates the clinical and cost-effectiveness of interventions independently”* and *“NICE is one of the toughest funding bodies, so I would be surprised if we didn’t get one of the best discounts anyway.”* This appears to be reflected by the UK government, as shown by its dissociation from the resolution approved by the WHA.

Additionally, when asked whether, in exchange for sharing their net price information, payers would prefer to observe the net price information of all European markets or within a group of markets similar to their own, their preference was for the latter option (Figure 6). Payers noted that sharing net price information between a group of countries could be more valuable than between all European markets both because *“it would also be important to share information with markets that have similar healthcare systems (e.g. no co-payment/universal coverage)”* and because *“it would be more efficient to start with transparency among a smaller group of markets and then later extend the procedure if it was having the desired effect.”* This reflects the perception of some challenges in sharing information between dissimilar markets and the concern that NPT might not be as beneficial as some stakeholders theorise. If payers were fully in support of greater NPT and considered that there would be no downsides, it is reasonable to assume they would want to see prices in all markets.

Figure 6: Payer level of interest in the net price information from all European countries or a group of countries



Source: CRA Payer Survey (2020)⁷⁵

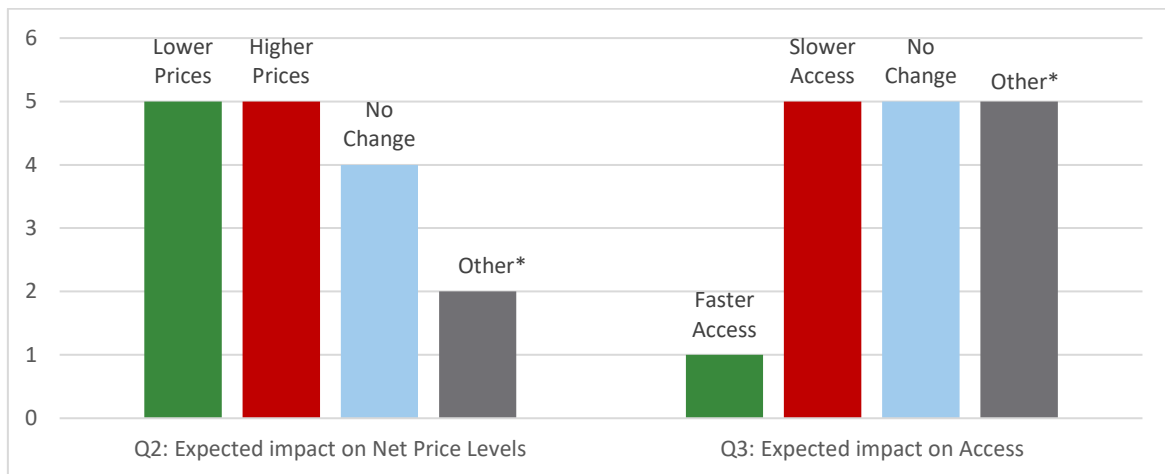
3.2. Most payers expect there would be negative consequences from greater NPT

The payer survey also asked respondents to indicate their expectations about greater NPT with regard to net prices and access in their market. Figure 7 shows an even split between payers who

⁷⁵ CRA Payer Survey: “Please indicate which of the following methods for increasing price transparency would be most attractive to you.”

expected greater NPT to result in higher prices and those who expected lower prices. However, a clear majority of payers expected greater NPT to lead to slower access (a minority expected faster access). This is in contrast to the results presented in Figure 4 that show the majority of respondents indicating their support for greater NPT. This contrast between the general support for transparency and the expected impact of greater NPT on net prices and access shows that it is “politically” difficult for anyone to disagree with increased transparency (a principle that generally has positive connotations) even when they predict negative consequences, and it is a confidential survey.

Figure 7: Payer expectations about the impact of greater NPT on net price levels and patient access (n = 16)



*Other: Respondents indicated that they could not predict the outcome or that there would be a mix of outcomes (e.g. both higher and lower prices) dependent on current price levels and product characteristics.

Source: CRA Payer Survey (2020)⁷⁶

It is clear that greater NPT will limit (or potentially negate) the use of confidential agreements, which could subsequently result in prices going up. Given the nature of international reference pricing (IRP) mechanisms used widely, not just in Europe but also throughout the world, public list prices are a mechanism that prevents a downward pricing spiral for medicines from being triggered. Without confidential discounts, payers believe they would not be able to achieve the same net prices that they currently do under the public list price. The belief that confidentiality allows markets to achieve better prices is supported by the literature: a recent peer-reviewed study summarises an anonymous survey of payer authorities from public or social health insurance systems in 11 developed countries (Australia, Austria, Canada, England, Germany, New Zealand, Norway, Scotland, Sweden, the Netherlands, and the United States (US Department of Veterans Affairs)). When questioned on

76

CRA Payer Survey. **Q2:** “What do you expect to happen (i.e. not what you would like to happen) to the prices of innovative medicines in your market, if the level of price transparency is increased in all European markets, including yours (so the confidential prices negotiated in your market are known to others) and, at the same time, assuming that pharmaceutical companies would strategically react to the disclosure of confidential agreements?” **Q3:** What do you expect to happen (i.e. not what you would like to happen) to the time to access innovative medicines in your market, if the level of price transparency is increased in all European markets, including yours (so the confidential prices negotiated in your market are known to others) and, at the same time, assuming that pharmaceutical companies would strategically react to the disclosure of confidential agreements?”

overall perceptions of the impact of negotiating confidential discounts on patented pharmaceuticals, the responses indicated that confidentiality is valued by almost all respondents (Table 11).⁷⁷

Table 11: Overall perceptions of the impact of negotiating confidential discounts on patented pharmaceuticals in 10 public and statutory health systems surveyed (n = 10)

What is the overall impact of confidential price discounts for patented pharmaceuticals from a local health system perspective?	# of respondents
Very beneficial	5
Somewhat beneficial	2
Neither beneficial nor detrimental	1
Somewhat detrimental	0
Very detrimental	0
No answer	2

Source: Morgan, S., Vogler, S., & Wagner, A. (2017). Payers' experiences with confidential pharmaceutical price discounts: A survey of public and statutory health systems in North America, Europe, and Australasia. *Health Policy*, 121(4), 354-362.

Interestingly, in the payer survey, many respondents who indicated their general support for greater NPT also indicated that they value their own confidentiality:

- As highlighted by one Dutch respondent, “*there is a prisoners dilemma*” where all markets would prefer the disclosure of net prices in other markets but would prefer to keep their own prices confidential.
- A small number of respondents justified their support for greater NPT based on the fact that more information will put them in more informed positions for negotiations. They indicated that having access to the net prices agreed in other countries would help to strengthen their negotiation position (Table 12).⁷⁸ However, even these respondents expressed reluctance to share the details of their own confidential agreements, because they believe that confidentiality allows them to achieve the best prices.

This apparent contradiction of payers both valuing confidentiality to achieve better prices and also expressing support for greater NPT shows why the debate on transparency is complicated and confusing. For any one country, NPT of the price in other countries would apparently be beneficial, but NPT of their own prices to other markets would not.

⁷⁷ Morgan, S., Vogler, S., & Wagner, A. (2017). “Payers’ experiences with confidential pharmaceutical price discounts: A survey of public and statutory health systems in North America, Europe, and Australasia.” *Health Policy*, 121(4): 354–362. doi: 10.1016/j.healthpol.2017.02.002

⁷⁸ Some argued the disclosure of manufacturer access strategies and increased information sharing about the effects of other pricing methods would also help them in their negotiations.

Table 12: Qualitative justification for supporting NPT based on increased information available for negotiation

Market	Quote
Germany	<i>"We would like to assess whether we took the right figures into account and to initiate potential renegotiations"</i>
Italy	<i>"It would disclose manufacturers' market access strategies"</i>
Netherlands	<i>"I assume we will be able to estimate the effects of the other [pricing] methods"</i>
Poland	<i>"[It is] possible to have some higher and lower prices where Poland is currently overpaying or underpaying. Same with access – it depends on the situation, which is currently unknown since prices are confidential."</i>

Source: CRA Payer Survey (2020)

The reason payers believed that greater NPT would have negative consequences is that they have anticipated the impact on company strategy that would inevitably follow. This, they argue, would have the opposite effect to that intended (price increases and decreased access instead of price decreases and increased access, Table 13).

Table 13: Qualitative justification for opposing greater NPT based on expected changes in industry strategy

Market	Quote
Italy	<i>"Italy is a reference country for others, so companies wish the shown price to be the highest. It will have a diffused inflationary effect"</i>
Portugal	<i>"We are assuming that price transparency would allow for a lower price. However, manufacturers knowing that the price would be shared would try to start with higher prices"</i>
Sweden	<i>"The initial strategic reaction of pharmaceutical companies might lead to price increases."</i>

Source: CRA Payer Survey (2020)

3.3. NPT will result in price convergence with negative consequences for national budgets, especially in lower-income countries

There was consensus among experts on the advisory board that greater NPT can be expected to result in the convergence of prices across European countries because of the effects of IRP. The expectation of price convergence is consistent with the economic literature. Sellers would be less willing to negotiate lower prices to avoid a downward pricing spiral⁷⁹ and prices could potentially align to price levels in markets with the highest willingness to pay (WTP) for medicines.⁸⁰ Experts highlighted that price convergence does not necessarily mean that all European prices would be exactly the same, but it would result in much less differentiation in the ‘price corridor’.

Potential scenarios for price convergence

Experts highlighted that without being able to see the current net price differentiation across markets (due to the largely confidential nature of current agreements that are made) it can be hard to predict the exact impact of price convergence on final price levels across markets. It was therefore noted that the nature of net price convergence would depend on what markets are actually paying for innovative medicines, considering which markets are paying the most and the least. This was also stated by several payers during the survey (Table 14), reflecting the fact that some payers may gain from increased NPT while other may lose (in terms of impact on national budget).

Table 14: Payers highlighted that the impact of greater NPT will depend on current net prices, which are confidential

Market	Quote
Poland	<i>“It is possible to have some higher and lower prices where Poland is currently overpaying or underpaying... it depends on the situation, which is currently unknown since prices are confidential.”</i>
Italy	<i>“I would expect no change in prices or access for 60% of products, but the other 40% could see lower prices and faster access where we are overpaying”</i>

Source: CRA Payer Survey (2020)

Discussion amongst experts and responses from the payer survey indicated that the reaction of both payers and the industry to the disclosure on net prices plays a vital role in understanding how the dynamics of greater NPT will evolve. Although it is possible to predict that there will be price convergence, the “winners and losers” from this and the impact on overall budgets depends on

79 Kyle, M.K. & Ridley, D.B. (2007). “Would Greater Transparency and Uniformity of Health Care prices Benefit Poor Patients?” *Health Affairs*, 26 (5): 1384–1391. DOI 10.1377/hlthaff.26.5.1384

80 Moira Dower, PVW Amsterdam, (2019). “Pressure for Price Transparency”, available at: <https://www.pvwamsterdam.com/single-post/2019/09/04/Pressure-for-Price-Transparency>

different factors and requires many different assumptions. As a result, experts suggested that the potential consequences of price convergence can be considered through a simulation model informed by similar models that analysed the impact of greater transparency on the sector of medical devices⁸¹ and in the wages market.⁸²

A key consideration, not in the remit of in this white paper, is the scenario that the US implements IRP. While the impact on price convergence is uncertain when considering Europe as a closed market (as done in this white paper), when the proposed changes to the US pricing system were factored in, there was consensus amongst experts at the advisory board that price convergence in countries being referenced by the US would be in the direction of US prices. This would result in a scenario in Europe where there are significantly more losers than winners from a national budget perspective, a scenario that should be given stronger consideration by advocates for greater NPT as this debate progresses.

Expected impact of price convergence

Assessments of the overall effect of greater NPT on national budgets should account not only for the strategic reaction of payers to increased information but also for the strategic reaction of manufacturers: in particular how the industry would be likely to adapt their commercial and pricing strategies to the new transparent environment where confidential discounts are not possible. In a situation of greater NPT, the economic literature highlights that pharmaceutical companies would have an incentive to avoid offering price concessions for a single market that would have a spillover impact in other potential more valuable markets from a commercial perspective.⁸³ For example, this was seen within the pharmaceutical industry upon the US government's adoption of the Most Favoured Customer clause mandating that prices offered to Medicaid must be at least equal to the lowest price being paid for the medicine elsewhere. This ultimately saw higher prices in non-Medicaid consumers in order to protect Medicaid prices.⁸⁴ While this is an example within just one market, Figure 8 illustrates how price convergence could result in price increases across markets, by considering two scenarios. In scenario A, the price is lowered to the lowest price. This would clearly benefit the higher-price market and have no negative consequences for the lower-price market. However, in reality, we might also expect the company pricing strategy to adapt so that the price in lower-income countries takes into account the consequence in the higher-income market. Scenario B shows the higher-price country gains at the expense of the lower-price country.

81 Grennan, M. (2013). "Price discrimination and bargaining: Empirical evidence from medical devices". *American Economic Review*, 103(1): 145–77.

82 Cullen, Z. B., & Pakzad-Hurson, B. (2019, May). "Equilibrium effects of pay transparency in a simple labor market". In EC (p. 193).

83 Shaw, B., & Mestre-Ferrandiz, J. (2020). "Talkin' About a Resolution: Issues in the Push for Greater Transparency of Medicine Prices". *Pharmacoeconomics*, 38(2): 125–134. doi: 10.1007/s40273-019-00877-3

84 Scott Morton, F. (1996). "The Strategic Response by Pharmaceutical Firms to the Medicaid Most-Favored-Customer Rules". Available at <https://www.nber.org/papers/w5717>

Figure 8: Simplified examples to illustrate the implications of abandoning differential pricing strategies

Assume two countries. Country X: higher-income country with a large population. Country Y: lower-income country with a smaller population. With confidential discounts, the price level in Country Y is lower, accounting for its lower ability to pay

	List price	Net price (after confidential discounts)	Patients	Company revenues
Country X	100	70	100,000	7,000,000
Country Y	100	50	10,000	500,000
TOTAL				7,500,000

Scenario A. Confidential discounts are disclosed and the company keeps the same discount for Country Y, to facilitate access. Country X therefore expecting the same level of discount as observed in Country Y

	List price	Net price (after transparent discounts)	Patients	Company revenues
Country X	100	50	100,000	5,000,000
Country Y	100	50	10,000	500,000
TOTAL				5,500,000

Scenario B. Confidential discounts are disclosed and the company applies the discount for Country X also in Country Y, despite this potentially resulting in no access in Country Y

	List price	Net price (after transparent discounts)	Patients	Company revenues
Country X	100	70	100,000	7,000,000
Country Y	100	70	-	-
TOTAL				7,000,000

From a commercial perspective, the company would prefer scenario B (which maintains the smaller discount of country X) over Scenario A (which uses the larger discount of country Y). However, Scenario B could lead to reduced/no access in Country Y due to the smaller discount.

Source: CRA

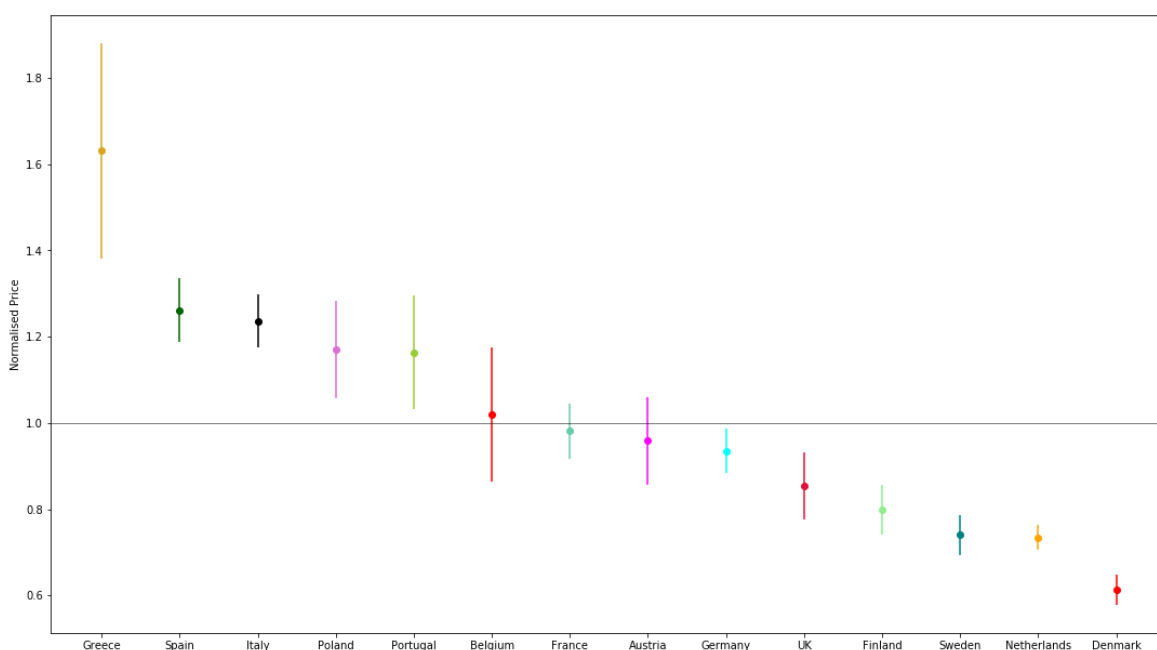
To examine how this might occur in Europe, a computational model was developed. The model simulates the effect of a counterfactual NPT policy on the net pharmaceutical prices negotiated in several European markets. In particular, it considers the case of an innovative pharmaceutical product facing no therapeutic competition. In a two-stage simulation design, first, countries negotiate with the manufacturer a national price both exhibiting a bargaining power resulting in a confidential rebate and a Nash equilibrium price obtained in each country for the quoted value-based price (VBP). Given the currently confidential nature of innovative medicine pricing, the computational model considers that the VBP (i.e. price obtained without transparency/under normal conditions) is the average of the published list prices for a selection of innovative medicines over the period 1996–2008 with a normalised, average confidential rebate of 30% uniformly set for all countries.⁸⁵ In the second stage, the model also assumes that there is full NPT, the bargaining power is unchanged and all markets will want to reference the lowest transparent price. In this situation, the manufacturer faces a reduced price in some markets, but this leads to a change in willingness to accept lower

85 Additional assumptions are made about the normalisation of each country market size (which was done taking OECD-reported country-level pharmaceutical spending and expressing each country's PPP market size as a percentage of the largest pharmaceutical spending country) and the nature of the manufacturer's marginal costs and profit margins.

prices in other markets. This effect can be expected since reduced profits in higher-income markets would need to be absorbed and therefore redistributed to lower-income markets.

The results of the computational model are shown in Figure 9. Markets such as Greece, Spain, Italy, Poland and Portugal could expect price increases under transparent conditions whereas, according to the model, higher-income markets such as Germany, the UK, Sweden, the Netherlands and Denmark could expect price decreases (price change below original). Interestingly, in these markets where prices are expected to decrease, the overall spend on pharmaceuticals as a proportion of healthcare spend is generally lower than in the markets that could expect price increases.^{86,87} At the extreme levels, some markets could see their prices increase (Greece) or decrease (Denmark) by as much as 60% should prices in Europe be made transparent. The results from this model do not take into account how purchasers would react. Indeed, it would seem economically irrational for countries suffering from such an increase in price levels to participate in a system with greater NPT. Therefore, we would not expect this simulated outcome to be sustainable.

Figure 9: Normalised price change under net price transparency in selected European markets



Source: Van Dyck, W., Riccaboni, M., & Swoboda, T. 2020. *Pharmaceutical net price transparency across European markets: Insights from a Multi-Agent simulation model*, Vlerick Policy Paper Series #13. Brussels, Belgium: Healthcare Management Centre, Vlerick Business School.

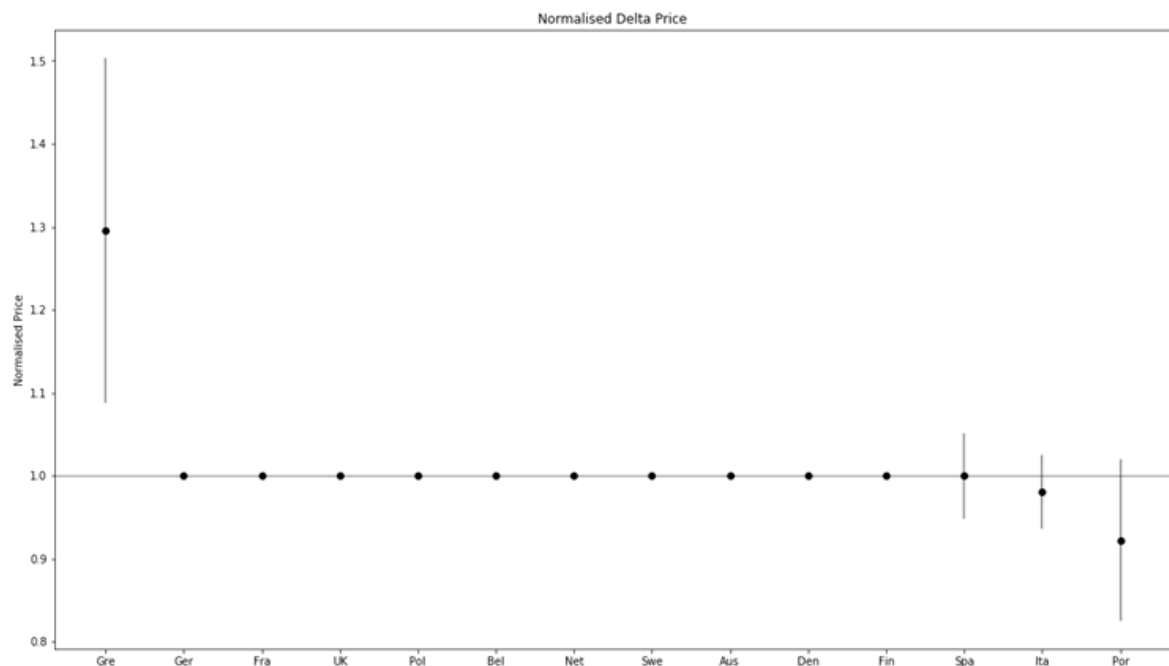
The computational model also analyses the scenario (discussed in some political debates) whereby NPT is not applied to all European markets but is instead adopted within a group (collaboration) of

86 Pharmaceutical spend in Denmark as a proportion of overall spend (6.4%) is one of the lowest in the world, whereas Greece lies on the opposite end of the spectrum (26.2%).

87 OECD (2019). "Pharmaceutical Spending as % of Health Spending". Available at <https://data.oecd.org/healthres/pharmaceutical-spending.htm>

markets. This is the case, for instance, of the Valletta Declaration Group, which has been considering how to increase the transparency of medicines pricing.⁸⁸ Although this avoids the transfer from the highest income to lowest, the same broad result occurs. In this case, the computational model shows that the benefit of having such a collaboration is inequitably distributed across the participating countries. The countries that had a higher than European average list price before the implementation of NPT within the group may benefit from it, while those that had a below European average list price would end up paying higher prices (Figure 10).

Figure 10: Normalised price change under net price transparency within a group of countries such as the Valletta Declaration



Source: Van Dyck, W., Riccaboni, M., & Swoboda, T. 2020. *Pharmaceutical net price transparency across European markets: Insights from a Multi-Agent simulation model*, Vlerick Policy Paper Series #13. Brussels, Belgium: Healthcare Management Centre, Vlerick Business School.

The simulation is inevitably a simplification of reality. There are many other possible scenarios, which depend on various market characteristics and dynamics (e.g. price elasticities, costs structure, price formation mechanisms). Further, this computational model also only considers NPT in a closed European system and does not consider the more extreme scenario in which markets such as the US are able to reference transparent European net prices. It is not possible to determine with any accuracy who benefits and who loses, but it is clear that lower-income countries that are able to negotiate lower prices will lose from NPT, and higher-income countries that are paying higher prices will benefit; and in a more extreme scenario, with European NPT affecting other market dynamics, it is likely that the majority of European countries will be losers.

Importantly, in addition to the impact on payer's budget, NPT will have an implication on patient access, possible leading to access delays (or even to no access at all) in some markets as predicted by economic theory.⁸⁹ On this aspect, the computational model finds that an NPT policy not only delays market access in lower-income countries but also has a negative impact on middle-income countries.⁹⁰ We will cover more extensively the implications of access delays for patients in Chapter 5.

89 Towse, A., Pistollato, M., Mestre-Ferrandiz, J., Khan, Z., Kaura, S., & Garrison, L. (2015). "European Union pharmaceutical markets: a case for differential pricing?" *International Journal of the Economics of Business*, 22(2): 263–275.

90 Van Dyck, W., Riccaboni, M., & Swoboda, T. 2020. Pharmaceutical net price transparency across European markets: Insights from a Multi-Agent simulation model, Vlerick Policy Paper Series #13. Brussels, Belgium: Healthcare Management Centre, Vlerick Business School.

4. The impact of NPT on the functioning of the market for innovative medicines

KEY FINDINGS

- **Greater NPT would facilitate a shift away from value-based pricing mechanisms and exacerbate the impact of international reference pricing (IRP).**
- **In order to achieve 'de facto' confidential discounts, pricing mechanisms that are not subject to NPT could be misused, which not only would be inefficient but also would disadvantage markets lacking the infrastructure and experience to facilitate their implementation.**
- **Public net prices are likely to reduce competition amongst sellers, potentially raising prices of new medicines in Europe.**
- **Greater NPT could reduce market attractiveness for investments.**

4.1. Greater NPT would alter the way in which pricing mechanisms are applied

Across European markets, payers use four main methods of controlling pharmaceutical prices: pricing negotiations, the use of value assessment and cost-effectiveness, reference pricing, and (rarely, some form of) profit controls. In reality, most systems are a form of hybrid using a number of different methods. As pharmaceutical pricing is a national competence, European countries take very different approaches. It is also worth noting that some markets use different methods for different medicines (for example, one method for orphan medicines and another for non-orphan medicines).⁹¹

Greater NPT is expected to alter the way in which these different pricing mechanisms are used. The effect on each pricing mechanism is expected to be different (Table 15): for example, greater NPT is expected to facilitate a shift away from value-based pricing mechanisms that rely heavily on HTA and lead instead to IRP mechanisms. Experts on the advisory board also highlighted that this could result in a situation where payers choose to determine innovative medicine prices based on whichever method allows them to achieve greater price reductions. In this situation, prices are decided without considering the value of a medicine and without transparency on the factors influencing the decision-making process. Additionally, this increased reliance on IRP ignores the specific value that one product can have in an individual country that may be different from the value in others (e.g. an anti-infective that is used in reserve in one market but needed earlier in the treatment paradigm in another due to higher epidemiology of resistant infections, or a product used to treat a genetic disease that is of higher prevalence in some geographies).

The conclusion that NPT will influence the way in which pricing mechanisms work is also supported by results from the payer survey. Under the assumption that greater NPT would be mandated at the European level and incorporated into European legislation, a significant majority of survey

91

Mrazek, M. F. (2002). "Comparative Approaches to Pharmaceutical Price Regulation in the European Union". *Public Health*, 43(2): 453-461.

respondents (11/16 respondents) indicated that they would expect their own pricing and reimbursement process to be updated to accommodate this change in legislation at the European level (i.e. to make the most of the now transparent price agreements being made in other European markets).⁹²

Table 15: Expected effect of greater NPT on the use of common pricing mechanisms

Target	Expected effect of greater NPT	
Effect on the use of IRP	▲ Increase	With greater NPT, the reliance of markets on IRP for setting medicine prices is expected to increase based on the increased level of price information available. Experts also agreed that markets currently using IRP as just a part of their price setting strategy may start to put more emphasis on IRP mechanisms, especially when it helps them to achieve lower prices.
Effect on the use of HTAs	No change	Markets that only use HTA to determine prices (Sweden and the UK) are expected to continue using the same methods to determine prices. What may change is the impact that these value-based prices have on price setting in other markets.
	▼ Decrease	With greater NPT, and the assumption that all markets wish to achieve the lowest prices possible, in markets that use both IRP and HTA to set prices, the importance of HTAs is expected to decrease given that value-based pricing is not expected to give markets the lowest price possible.
Effect on the use of confidential discounts	X Cease	In the context of greater NPT, confidential discounts will not be possible.

Source: CRA Expert Advisory Board

Given the variation in the ways in which the different pricing mechanisms are used across markets, the changes introduced by greater NPT are expected to impact markets in different ways. Very few markets rely solely on one type of pricing mechanism (for example, Poland uses cost-effectiveness calculations as just one part of its several-step price calculation method, and France only uses IRP mechanisms when drugs are granted an ASMR III⁹³ or above); however, almost all European

⁹² CRA Payer Survey. Question: "If increased net price transparency was introduced in Europe, would you expect the pricing and reimbursement process in your market to be updated to accommodate this change in legislation?"

⁹³ An ASMR (Amélioration du Service Médical Rendu / Improvement of the Medical Benefit) is granted by the French clinical assessors; an ASMR III is considered a relatively high ASMR rating (the scale goes from I (highest) to V (lowest)) and the referencing of other markets pricing in this instance considered a 'reward' versus the usual price negotiation process

markets (with the exception of the UK and Sweden⁹⁴) use IRP mechanisms to some extent to inform price setting processes:

- *Focusing first on markets that do not use any IRP mechanisms to determine prices (the UK and Sweden):* In the payer survey, payers from these markets highlighted that they expect greater NPT to have a lesser effect on their pricing process – it is not expected that they will adopt IRP due to greater NPT. However, we also need to take into account the impact of other countries using UK and Swedish prices. Therefore, although the UK and Sweden have previously acted independently, with greater NPT their influence on other markets would change, which could reduce their ability to negotiate prices. Given the reduced ability to use confidential rebates, it is likely that alternative approaches would be considered.
- *Considering markets that use some form of IRP:* They will be affected differently. Some markets use IRP as their main pricing determinant (e.g. Austria, Bulgaria, Norway, Romania), and others use IRP to provide supportive information for the negotiation process (e.g. Italy, Poland, Spain).⁹⁵ In markets that currently use a combination of HTA and IRP to inform (or determine) price levels, experts hypothesised scenarios where payers give greater or lesser importance to different mechanisms in their pricing process depending on what would result in a lower price. This arbitrary selection of pricing mechanisms would result in increased uncertainty on how pricing is determined. This builds on the observation above, that an increase in NPT (price transparency) may result in a decrease in pricing transparency (i.e. transparency on the rationale behind pricing and reimbursement decisions).

Experts also theorised that with greater NPT, some European markets would attempt to form coalitions and cross-country collaborations to put themselves in stronger negotiating positions and increase their bargaining power. Already, there are examples of cross-country collaborations across Europe applied to HTAs, reimbursement decisions and procurement, although none are used consistently for all medicine approvals (e.g. the BeNeLuxA-I coalition and the Valletta Declaration group). In theory, these collaborations can be used to positive effect in the case of innovative medicines, particularly advanced therapy medicinal products (ATMPs), improving efficiency in assessment processes and decreasing time to access, but little empirical evidence of this currently exists. In an environment of greater transparency, countries could be forced to explore these alternative approaches more seriously as tools to gain efficient access to innovative medicines.

4.2. Greater NPT could encourage the misuse of payment mechanisms

Given the shared desire between payers and manufacturers to provide patients with access to innovative medicines, if they are not able to use confidential discounts, experts highlighted that they may consider other ways to gain ‘informal’ confidential discounts through arrangements that are not intended for this purpose, for example, MEAs. According to the definition used by the OECD, MEAs are “*arrangements between a manufacturer and payer/provider that enable access to*

94 Rémuzat, C., Urbinati, D., Mzoughi, O., El Hammi, E., Belgaied, W. & Toumi, M. (2015). “Overview of external reference pricing systems in Europe”. *Journal of Market Access & Health Policy*, 3:1, DOI: 10.3402/jmahp.v3.27675

95 Rémuzat, C., Urbinati, D., Mzoughi, O., El Hammi, E., Belgaied, W. & Toumi, M. (2015). “Overview of external reference pricing systems in Europe”. *Journal of Market Access & Health Policy*, 3:1, DOI: 10.3402/jmahp.v3.27675

(coverage/reimbursement of) a health technology".⁹⁶ While these can be financial agreements, many MEAs are intended to be used to manage uncertainty regarding the clinical performance of a medicine, not as arrangements with the explicit objective to provide a discount on a health technology. The literature highlights that these types of MEAs should only be used when HTAs identify issues or concerns that are material to a coverage decision and traditional reimbursement pathways are inappropriate.⁹⁷

In the case of greater NPT, payers could look to use performance-based MEAs, such as coverage with evidence development (CED) agreements, to achieve an ex-post unobservable (confidential) discount. The original purpose of CED agreements was to provide conditional coverage to new technologies with limited clinical data and incentivise the collection of real world evidence (RWE) to provide more certainty to physicians and payers on the clinical and/or cost-effectiveness impact.⁹⁸ While the collection of RWE indeed has value in many scenarios, using such performance-based MEAs with the primary objective of achieving a financial discount would be against the intended purpose of such agreements. Furthermore, it is recognised that agreeing and implementing performance-based MEAs is resource intensive, due to the time required to negotiate the agreement, the collection of additional evidence and the future monitoring and re-assessment of the product if required. As a result, most stakeholders consider that MEAs are to be used only when required and that using such agreements in place of confidential discounts would be inefficient and could delay patient access. Further to this, with greater NPT, payers should be aware of the importance of justifying their use of MEAs, to potentially mitigate against concerns of misuse.

Lastly, not all countries use MEAs to the same extent. Markets with a lack of infrastructure or a lack of experience in implementing more sophisticated payment models have less ability to (mis) use MEAs. Some of the key challenges associated with the implementation of MEAs include lack of logistical capabilities and difficulty to incorporate into inflexible reimbursement frameworks.^{99,100} In general, the implementation of MEAs requires the adoption of legal provisions allowing payers to use them, and their incorporation into the pricing and negotiation process (usually coupled with HTA methodologies to link the MEA to value and uncertainty around value). Moreover, there is a need for data infrastructure, requiring the establishment of patient registries and electronic patient records (which also require privacy protection rules and implementation of a recording system compliant with the European General Data Protection Regulation, GDPR).¹⁰¹ These challenges could be expected to be exacerbated in relatively lower-income markets, which generally have fewer resources to support the implementation of complex agreements. Literature reviews have also shown how lower-

96 Wenzl, M. and S. Chapman (2019). "Performance-based managed entry agreements for new medicines in OECD countries and EU member states: How they work and possible improvements going forward". OECD Health Working Papers, No. 115, OECD Publishing, Paris. Available at <https://doi.org/10.1787/6e5e4c0f-en>

97 Klemp, M. and Frønsdal, K.B. (2011). "What principles should govern the use of managed entry agreements?" *International Journal of Technology Assessment in Health Care*, 27(1): 77–83.

98 Trueman, P., Grainger, D. L., and Downs, K. E. (2010). "Coverage with Evidence Development: applications and issues". *Int J Technol Assess Health Care*, 26(1): 79–85. DOI: 10.1017/S0266462309990882.

99 Carbonneil, C. et al. (2009). "A common policy framework for evidence generation on promising health technologies".

100 Montilva, J. et al. (2016). "Adoption of Managed Entry Agreements in established and emerging markets".

101 CRA analysis (2018) "The experience of managed entry agreements (MEAs) in Europe".

income countries are less likely to have experience in using MEAs, particularly with regard to performance-based MEAs, which have been primarily implemented in higher-income countries as they require more capacities for data collection, monitoring and evaluation. Many reports show that MEAs are used to a greater extent in western European markets and to a lesser extent in Central and Eastern European markets.¹⁰² Therefore, with greater NPT, lower-income markets would likely have fewer options to adopt an ‘informal’ confidential discount and subsequently be disadvantaged from the potential misuse of pricing mechanisms. To the extent that MEAs mitigate the negative impact of NPT, this supports the point that greater NPT is more likely to disadvantage lower-income markets.

4.3. Greater NPT could adversely affect competition in the pharmaceutical industry

The pharmaceutical market is unusual when compared to other industries, partly due to its focus on innovation and dynamic competition. There are often relatively few competitors, due to the nature of the products (innovative medicines) that are being sold during the period of patent protection, and therapeutic competition between differentiated products results in new prices falling over time to the benefit of payers and ultimately patients.¹⁰³ Further to this, the pharmaceutical market can generally be considered to be a monopsony, with most of the European markets operating through a single payer body. The pharmaceutical industry has already been highlighted as one of the riskiest industries in which to invest, despite the widely held belief that it is excessively profitable,¹⁰⁴ and it is likely that the impact of greater NPT will negatively affect the nature of competition within the industry, potentially leading to further uncertainty.

In an environment of greater NPT, sellers will be less likely to offer a lower price to buyers, as negotiations with other purchasers will be affected, and because their competitors will be able to observe the price being offered. The consensus across the experts on the advisory board, as well as in the literature, was that this will reduce competition compared to today.¹⁰⁵ And lastly, in the payer survey, the negative effects of greater NPT on competition were mentioned by some respondents: for example, one payer from Italy noted, “It [greater NPT] would disclose manufacturers’ market access strategies, impairing the level of competition in the arena”.¹⁰⁶ The impact of competition on the decrease of prices of innovative medicines has been seen in many instances, most evidently in Hepatitis C, where across European markets intense competition has

102 Castro, H. E., Malpica-Llanos, T., Musila, R., Konduri, N., Amaris, A., Sullivan, J. And Gilmartin, C. (2019). “Sharing knowledge for policy action in low- and middle-income countries: A literature review of managed entry agreements”, *Medicine Access @ Point of Care*. Available at <https://journals.sagepub.com/doi/full/10.1177/2399202619834246>

103 Roediger, A., Wilsdon, T., Haderi, A., Pendleton, K., & Azais, B. (2019). “Competition between on-patent medicines in Europe”. *Health Policy*, 123(7): 652–660.

104 David Taylor, *The Pharmaceutical Industry and the Future of Drug Development*, in *Pharmaceuticals in the Environment*, 2015, pp. 1–33. Available at <https://pubs.rsc.org/en/content/chapterhtml/2015/bk9781782621898-00001?isbn=978-1-78262-189-8>

105 Shaw, B., & Mestre-Ferrandiz, J. (2020). “Talkin’ About a Resolution: Issues in the Push for Greater Transparency of Medicine Prices”. *Pharmacoeconomics*, 38(2): 125–134. doi: 10.1007/s40273-019-00877-3

106 CRA Payer Survey (2020).

led to sharp decreases in prices and overall spending. Payers reported declines in spending despite the approval and launch of new medicines, indicating lower net prices at launch (although public list prices remained consistent).¹⁰⁷ Even further to this, the intense competition resulted in a new model of therapeutic tendering to be developed in England, requiring manufacturers to submit prices based on their achievable market share, resulting in further price decreases.¹⁰⁸

The role of transparency in competition has been examined by academic and competition authorities.¹⁰⁹ Competition law has been constructed to ensure that companies do not share valuable information that could cause sellers to gravitate to higher prices or collusive arrangements.¹¹⁰ Especially in industries where the pre-existing level of transparency is low, information holds more value and therefore effects on the market upon disclosure can be exacerbated.¹¹¹ The advisory board discussed the degree to which we could learn from other industries and whether increased collusion following the implementation of price transparency measures have been seen. Although the pharmaceutical market is different in terms of the reliance on dynamic competition, these lessons from other industries show how collusion is facilitated by a transparent market, and although lessons from other industries should be used with care, they should not be ignored. In fact, economists often argue that collusion is more difficult with large numbers of traders,¹¹² and therefore in industries where competition is concentrated (as in the pharmaceutical industry) the risk of tacit collusion is increased. This has also been noted by the OECD, which noted that in sufficiently concentrated markets, *“the competitive risks of increased price transparency [...] have not always been sufficiently appreciated by government policy makers. There have been instances where government mandated increases in price transparency seemed to have produced higher rather than lower prices”*.¹¹³ It is important to notice the role that the degree of market concentration plays in the negative impact of increased price transparency: In more competitive markets, price transparency can also deliver benefits to the consumers in terms of increased competition; this is been the case, for instance, with digital platforms for online

107 Roediger, A., Wilsdon, T., Haderi, A., Pendleton, K. and Azais, B. (2019). “Competition between on-patent medicines in Europe”. Available at <https://www.sciencedirect.com/science/article/pii/S0168851019301289>

108 Hawkes, N. (2019). “NHS England finalises procurement to eliminate hepatitis C”. Available at <https://www.bmj.com/content/365/bmj.l1994.short>

109 Austin, A. & Gravelle, J. (2007). “Does Price Transparency Improve Market Efficiency? Implications of Empirical Evidence in Other Markets for the Health Sector”. Congressional Research Service.

110 Shaw, B., & Mestre-Ferrandiz, J. (2020). “Talkin’ About a Resolution: Issues in the Push for Greater Transparency of Medicine Prices”. *Pharmacoeconomics*, 38(2): 125–134. doi: 10.1007/s40273-019-00877-3

111 European Commission. Guidelines on the applicability of Article 101 of the Treaty on the Functioning of the European Union to horizontal cooperation agreements. Communication from the Commission, 2011/C 11/01. 2011. p. 17. [https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52011XC0114\(04\)](https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52011XC0114(04)) .

112 Austin, A., & Gravelle, J. (2007). Does Price Transparency Improve Market Efficiency? Implications of Empirical Evidence in Other Markets for the Health Sector. Congressional Research Service.

113 OECD (2001). “Price transparency”. Policy Roundtables DAFPE/CLP(2001)22 11 September 2001. Available at: <https://www.oecd.org/competition/abuse/2535975.pdf>

purchases.¹¹⁴ However, in industries facing a certain degree of market concentration (such as the innovative pharmaceutical industry), experience has shown that greater NPT can facilitate collusive behaviours, ultimately leading to higher prices.^{115,116,117,118,119}

4.4. Greater NPT could affect decision-making regarding international investments

According to experts, political decisions to increase the level of price transparency could also send a negative signal to national and international investors and influence the location of future investments. This effect would be provoked by the operationalisation of increased price transparency and the implications this can have on existing contracts, in both economic and legal terms. In economic terms, introduction of greater transparency would challenge the commercial value of existing procurement contracts: it would create an artificial differentiation between prices negotiated before and after transparency. There would also be questions on whether prices in older contracts should be updated to reflect the new transparency rules and to ensure fair therapeutic competition with products launched after the introduction of greater NPT. This would increase the uncertainty for the commercialisation of products, potentially destabilising market access pathways.¹²⁰ In legal framework terms, manufacturers may face a situation where they would be requested to disclose the net prices in markets where these are protected by confidential agreements with the local payers. In this circumstance, the delegitimisation of existing contracts would negatively affect the strength of the legal environment in the country implementing greater NPT, making it a riskier location for investments.¹²¹ Overall, the lack of attention to how greater NPT can destabilise the incentives for innovation, and policymakers failing to recognise these implications for the pharmaceutical industry, would reduce a country's credibility, ultimately impacting the attractiveness of a market as a destination for investments.¹²²

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- 114 Paul Belleflamme & Martin Peitz, 2019. "The Competitive Impacts of Exclusivity and Price Transparency in Markets with Digital Platforms," CRC TR 224 Discussion Paper Series crctr224_2019_137, University of Bonn and University of Mannheim, Germany.
- 115 Albaek, S., Mollgaard, P. and Overgaard, P.B. (1997). "Government-Assisted Oligopoly Coordination? A Concrete Case". *The Journal of Industrial Economics*, 45(4): 429–443. Available at <https://www.jstor.org/stable/2950610>
- 116 Luco, F. (2019). "Who Benefits from Information Disclosure? The Case of Retail Gasoline." *American Economic Journal: Microeconomics*, 11 (2): 277–305.
- 117 Albach, H. (1996). "The UK agricultural tractors information exchange system" in Albach, H., Jin, J. Y., and Schenk, C. (Eds.). "Collusion through information sharing? New trends in competition policy". ISBN 3-89404-157-9, Edition Sigma, Berlin.
- 118 OECD (2010). "Policy Roundtables: Information Exchanges Between Competitors under Competition Law".
- 119 United States v. Airline Tariff Publishing, Civil Action No. 92-2854, (D.D.C. filed Dec. 21, 1992).
- 120 Bailey, N. (2018). Exploring the relationship between institutional factors and FDI attractiveness: A meta-analytic review. *International Business Review*, 27(1): 139–148.
- 121 Czarnitzki, Dirk and Toole, Andrew A. (2006). Patent Protection, Market Uncertainty, and R&D Investment. ZEW – Centre for European Economic Research Discussion Paper No. 06-056, Available at SSRN: <https://ssrn.com/abstract=925621>.
- 122 Nera Economic Consulting (2007). "Key factors in attracting internationally mobile investments by the research-based pharmaceutical industry". A report prepared for the UK Trade and Investment and the Association of the British Pharmaceutical Industry.

In addition, if NPT affects product availability it could the adversely affect the possibility of conducting clinical trials in some of the European markets.¹²³ In this case, the latest innovations may not be available to patients (at least for a period of time) as ‘standard of care’ treatment for their condition. Consequently, other pharmaceutical manufacturers would be unable to conduct clinical trials in those countries that do not have access to the latest innovations which should be used as standard of care for the control arm of the trials.^{124,125}

123 This topic is extensively discussed in the next chapter.

124 Ashley, M. Y., Balasubramaniam, B., Offringa, M., & Kelly, L. E. (2018). “Reporting of interventions and ‘standard of care’ control arms in pediatric clinical trials: a quantitative analysis”. *Pediatric Research*, 84(3): 393–398.

125 Fogel, D. B. (2018). “Factors associated with clinical trials that fail and opportunities for improving the likelihood of success: a review”. *Contemporary clinical trials communications*, 11, 156–164.

5. The impact of NPT on patients access to different types of innovative medicines

KEY FINDINGS

- **NPT is likely to exacerbate differences in patient access rather than reduce inequalities.**
- **The impact will vary by therapeutic area. The impact is likely to be greatest where value to patients and market potential vary significantly for other reasons such as the degree of unmet need. This is likely to increase inequality for orphan medicines and transformative medicines.**

5.1. Access delays are likely to differ across markets

As discussed in Section 3.3, price convergence as a result of greater NPT is likely to disproportionately affect lower-income markets as price increases in these markets would be a natural consequence of potential price reductions in higher-income markets. This is likely also to lead to lower access in relatively lower- and middle-price countries, which can be explained in different ways:

- Diminished use of differential pricing. The ability to offer differential prices across markets is seen as critical for improving access to medicines.¹²⁶
- Or simply, that relatively lower-income countries will face higher prices, and given limited national resources dedicated to health, this will limit access to innovative medicines.

Consistent with economic theory, price convergence is expected to lead to access delays and potentially fewer product launches, especially in lower-income markets.^{127,128} This arises due to IRP and the impact IRP has on the strategic behaviour of the industry. In some cases payers will decide to delay price negotiations until prices in other markets are available, and in others the use of IRP provides incentives to manufacturers to launch drugs in an order that will protect their prices.^{129,130}

126 Yadav, P. for The U.K. Department for International Development (DFID), (2010). "Differential Pricing for Pharmaceuticals: Review of current knowledge, new findings and ideas for action". Available at <http://hsrii.org/wp-content/uploads/2014/05/diff-pricing-pharma.pdf>

127 Kyle, M.K. & Ridley, D.B. (2007). "Would Greater Transparency and Uniformity of Health Care prices Benefit Poor Patients?". *Health Affairs*, 26 (5): 1384–1391. DOI 10.1377/hlthaff.26.5.1384

128 Shaw, B., & Mestre-Ferrandiz, J. (2020). "Talkin' About a Resolution: Issues in the Push for Greater Transparency of Medicine Prices". *Pharmacoeconomics*, 38(2): 125–134. doi: 10.1007/s40273-019-00877-3

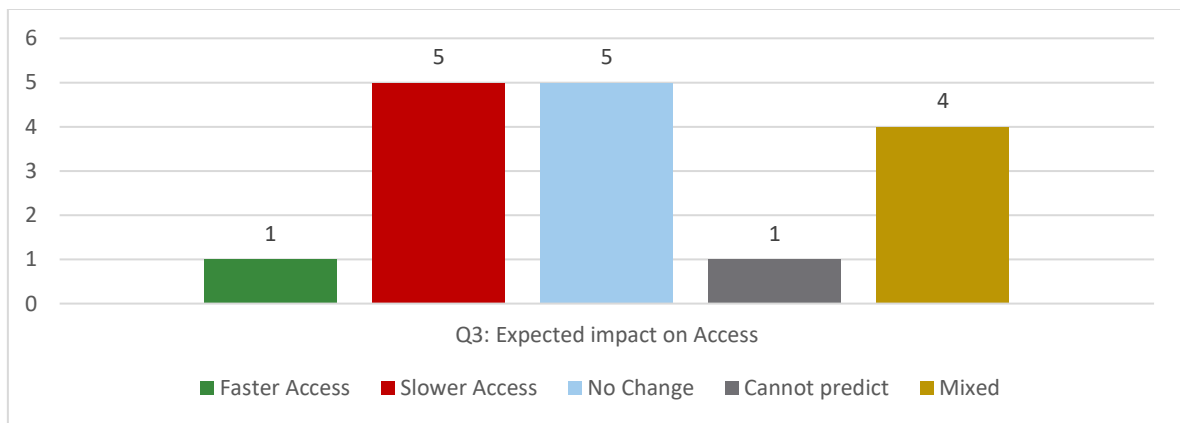
129 Zamora, B., Maignen, F., O'Neill, P., et al. (2019). "Comparing access to orphan medicinal products in Europe." *Orphanet J Rare Dis* 14, 95. Available at <https://doi.org/10.1186/s13023-019-1078-5>

130 Kanavos, P., Fontrier, A., Gill, J., & Efthymiadou, O. (2020) "Does external reference pricing deliver what it promises? Evidence on its impact at national level". *Eur J Health Econ* (21): 129–151. Retrieved 29 January, 2020, from <https://link.springer.com/article/10.1007/s10198-019-01116-4>

Further, markets may also use access delays as a negotiation lever to reduce prices (the value of a drug decreases the closer it gets to its patent expiry date).¹³¹ Experts highlighted that with greater NPT, price convergence (leading to increased prices especially in lower-income markets) and increased dependence on IRP mechanisms could exacerbate access delays. As a result, patients in lower-income markets are likely to incur greater access delays for medicines than they do currently.

A larger proportion of payers questioned in the survey indicated they would expect slower access to medicines (n = 5), whereas just one respondent indicated they would expect faster access (Figure 11). Many payers also indicated they would not expect any change in current access (n = 5) even when they did expect there to be changes to the prices. In particular, payers in Germany explicitly stated that they would not expect access to be delayed at all since immediate access (during the free pricing period) is a “cornerstone of drug policy in Germany”.¹³²

Figure 11: Payers were undecided as to the impact of greater NPT on access but did not believe access would improve



Source: CRA Payer Survey (2020)

The delay also occurs because of the impact on budgets and the strategic behaviour of payers. In markets where prices are expected to increase (lower-income markets currently paying lower prices and markets achieving significant confidential discounts compared to the highest-income / highest-price markets), it may not be possible for payers to agree to this higher price for a medicine, but it also may not be possible for the industry to sustainably offer a lower price due to the potential IRP implications in an environment of NPT.¹³³ This may mean that pricing agreements in lower-income markets are not able to be reached, resulting in a delay to access for several years until price erosion over time has brought the convergent European price to a level where they are able to pay. Figure 12 shows, in a simplistic and illustrative way, how offering different prices to markets with different budget constraints allows all markets to afford a product according to their ability to pay. In the case of price convergence, only one market can afford the price and therefore markets with stronger

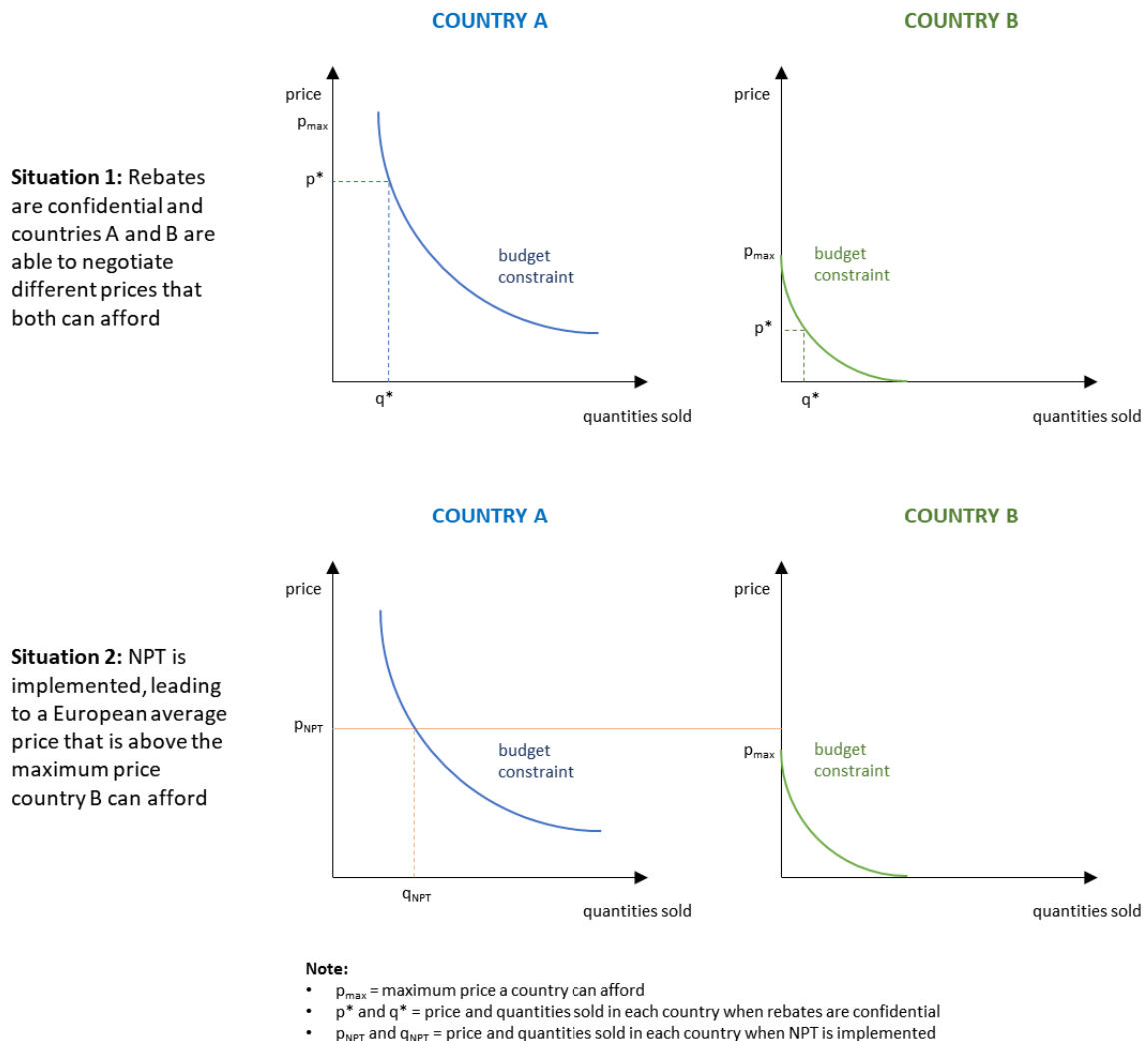
131 CRA Expert Advisory Board (2020).

132 CRA Payer Survey (2020).

133 Van Dyck, W., Riccaboni, M., & Swoboda, T. 2020. Pharmaceutical net price transparency across European markets: Insights from a Multi-Agent simulation model, Vlerick Policy Paper Series #13. Brussels, Belgium: Healthcare Management Centre, Vlerick Business School.

budget constraints will find themselves now unable to afford drugs and will see forced delays to access.

Figure 12: Price convergence means that countries with more stringent budget constraints will be kept out of the market and see increased delays to access



Illustrative representation: an accurate economic representation would consider additional market characteristics and dynamics (e.g. price elasticities, costs structure, price formation mechanism). However, the outcome from Situation 2 (i.e. no access in country B) represents an actual outcome that is possible under given circumstances.

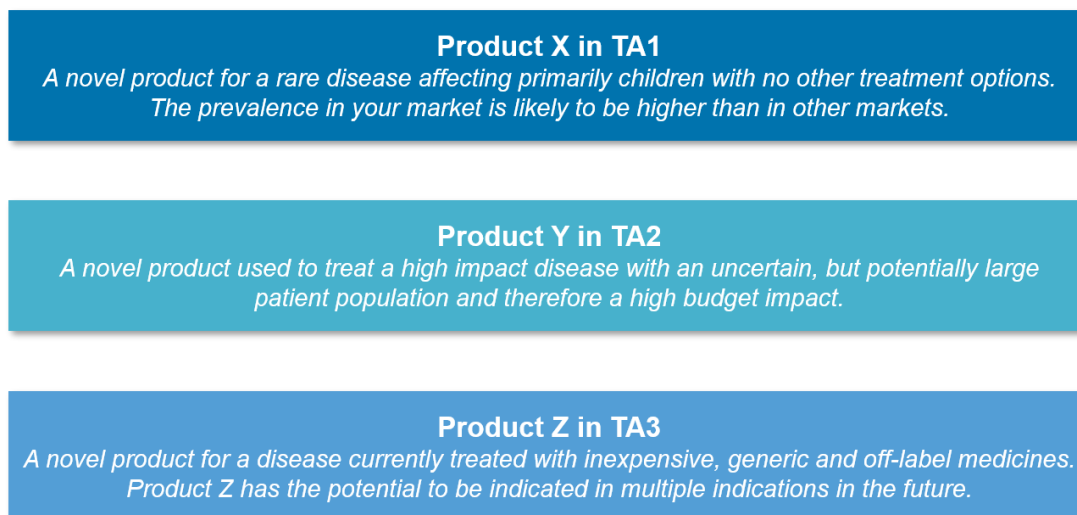
Source: CRA

5.2. Access delays are more likely for innovative products

The payer survey explored whether payers had different expectations about the impact of greater NPT on price and access of three different products in three different therapy areas (TAs) (Figure

13). In most cases answers remained consistent, indicating minimal expected changes in access across the three therapy areas.¹³⁴

Figure 13: Three products in three TAs were explored during the payer survey



Source: CRA Payer Survey (2020)

Experts on the advisory board additionally highlighted that while the three scenarios were different, each of the hypothetical products still represented a significant innovation, hence the similar expectations about price and access implications. Experts suggested instead that if the difference between the level of innovation of the three products was more pronounced, there would be significant differences in the impact on both price and access. Namely that with greater NPT, the more innovative products would likely be subject to longer access delays.¹³⁵

We consider the most innovative products and the products facing more therapeutic competition in turn. For the most innovative products, it is likely that value varies across countries. This outcome could depend on diagnostic structure or centres of excellence that do not exist in lower-income countries (hence the value delivered can be higher in markets with more advanced infrastructures). The volumes in the lower-income markets are also likely to be very small relative to the sales in higher-income countries. So, any impact of NPT will be exacerbated (given the commercial incentives to secure access in the higher-value / higher-volume markets). In this case, we might expect NPT to have a very strong impact on patient access, increasing the significant differences in access we already observe today.

If products are in a more mature class with competing products, we might expect the price difference between the higher- and lower-income countries to be smaller, reflecting the impact of competition in the higher-income countries and the increased bargaining power of the purchaser. Given that the differences in value across countries might be less pronounced, as it is less reliant on investment in the healthcare infrastructure, we would expect the impact on NPT to be less. The impact of any delay

134 CRA Payer Survey (2020).

135 CRA Expert Advisory Board (2020).

on lower-income countries will also be smaller, as there are a number of different products that can be used to serve patient needs.

This argument can be extended further. If we consider off-patent medicines, we would like prices to be determined by competition, with the result that prices should reflect the cost of these medicines. If competition works less well in some markets than others, NPT could share information on the price of off-patent medicines where it works effectively. In fact, some literature goes so far as to say that price transparency and uniformity could be beneficial in the generic drug market as this would encourage prices to reflect unit costs across markets.¹³⁶

5.3. Greater NPT could affect the development of new medicines

While the overall effects of greater NPT on industry revenues are hard to predict in the long term (and represent the mirror impact of national budgets discussed in Chapter 3), it is clear that NPT links different markets more closely together. The investment in innovative medicines is long and risky and involves companies anticipating how price and reimbursement systems will evolve across countries and regions – increased uncertainty will affect decision-making on long-term investments.¹³⁷

The experts on the advisory board warned of the implications of looking at NPT only through a European lens. If we consider the global breakdown of sales of the pharmaceutical market in 2019, European sales accounted for 22.9% of global sales, 48.7% came from the US and Canada, 7.2% from Japan and the remainder from the rest of the world.¹³⁸ In reality, these markets are already interconnected. Many markets reference European list prices to set their own medicine prices (e.g. Australia, Canada, Japan) and others are discussing implementing such rules (e.g. the US). With greater NPT, the prices agreed in European markets could have a greater impact on global pharmaceutical sales, especially if the US proceeds to implement IRP of European net prices.¹³⁹ It is also important to consider that if prices in Europe influence the prices in other markets, particularly the US, this could have a significant impact on willingness to negotiate prices in Europe and could affect access to medicines. Greater European NPT could firstly increase the risk of reducing revenues available for R&D investment, harming patients all over the world from a health outcomes perspective. Alternatively, in order to maintain current private sector R&D investment levels, European markets could see higher prices, thus harming payers through higher prices and/or patients through reduced access to treatment. Again, this is likely to impact the most novel medicines to the greatest extent.

136 Kyle, M.K. & Ridley, D.B. (2007). "Would Greater Transparency and Uniformity of Health Care prices Benefit Poor Patients?". *Health Affairs*, 26 (5): 1384–1391. DOI 10.1377/hlthaff.26.5.1384

137 Al-Thaqeb, S. A. and Algharabali, B. G. (2019). "Economic policy uncertainty: A literature review". *The Journal of Economic Asymmetries*.

138 EFPIA (2020). "The Pharmaceutical Industry in Figures: Key Data". Available at https://www.efpia.eu/media/554521/efpia_pharmafigures_2020_web.pdf

139 US Government website (2019). "Lower Prescription Drug Costs Now". Available at: <https://www.speaker.gov/sites/speaker.house.gov/files/HR3%20Backgrounder%2010.2.19.pdf>

6. Conclusions

KEY CONCLUSIONS

- **The NPT debate (and other transparency debates) are largely politicised; greater consideration should be given to the likely impact of policy changes on society based on economic theory and literature evidence.**
- **Greater NPT in Europe is likely to have negative consequences for patients, payers' budgets and the functioning of the market for innovative biopharmaceuticals.**
- **Greater NPT in Europe must also be considered in the wider context of the policy in other key markets, in particular in markets that reference (or plan to reference) European prices.**

In this report we have tried to document evidence on the impact of NPT. It draws on a literature review, a survey of European payers, an advisory board of economic experts representing many European countries, and a new economic simulation model. It is clear that greater NPT will not have a uniform impact across countries but has the potential to cause unintended negative consequences both in the short and long term for patients, payers' budgets and the functioning of the market for innovative biopharmaceuticals, if implemented without stringent measures to mitigate against the potential risks.

The initial ramification of price convergence upon disclosure of confidential price information (which is widely supported by the literature and now by a robust economic simulation model) would be likely to result in price increases in markets that are currently paying below the European average (assumed to be typically lower-income markets). This will have negative impacts not only on payers and national budgets, particularly in lower-income markets, but also on patients through delayed patient access. In addition, the functioning of the market is likely to be adversely affected: the way in which pricing mechanisms are used is expected to change (potentially resulting in the misuse of some pricing mechanisms), competition could decrease, and this will increase uncertainty, potentially impacting innovation.

There is divergence of the political debate on greater NPT and the technical debate on the impact of greater NPT as well as frequent conflation within the political debate of the principles of 'price transparency' and 'pricing transparency'. Many stakeholders, including payers, industry, the general public and technical experts, recognise the value of transparency in decision-making around innovative medicine prices (pricing transparency). However, the impact of greater price transparency (i.e. greater NPT) on patients, healthcare spending and innovation needs to be taken into account.

Whether it is possible to increase transparency, improving trust and confidence, without the negative consequences on patients, the healthcare system and innovation, needs careful consideration. This should involve a multi-stakeholder consultation process to ensure that all implications are understood and accounted for and appropriate mitigation strategies put in place. Experts highlighted that a key potential mitigation would be to have prior agreement amongst participating markets on Ramsey Pricing levels to ensure price differentials across participating markets are maintained. However, experts also stressed that reaching such agreements would be politically challenging although considered theoretically possible and fair through advanced discussions and strict laws to ensure individual states do not renegotiate lower prices upon publication of prices in other markets.

This concept has been typified by recent events in Italy: a legislative decree passed by the government calling for the disclosure of negotiated agreements was later followed by practical implementation guidelines from the Italian payer authority, AIFA, which subsequently accounted for and protected existing confidential agreements (Case study). This example shows how consideration of the technical ramifications of NPT is important before passing legislation that may endanger existing systems that are in place to ensure and protect the functioning of the biopharmaceutical market.

Case study of the Italian market: AIFA's implementation guidelines for the Pricing & Reimbursement Decree

In July 2020, a Pricing & Reimbursement Decree was published in the 'Gazzetta Ufficiale della Repubblica Italiana' based on legislation approved by the previous Ministry of Health and Ministry of Economy and Finance. Most notably, this decree stated that the manufacturer must provide information about "... *marketing, consumption and the reimbursement in other countries ... including any further negotiation agreements*" in order to begin the reimbursement negotiation process.¹⁴⁰

In August 2020, AIFA followed up with guidelines on how this decree is to be implemented and clearly upholds the confidentiality of pricing agreements made in other markets. Manufacturers are only requested to share negotiated discounts if these are non-confidential.¹⁴¹

This reaction from AIFA to the new legislation shows that payers in Italy recognise the value of confidentiality and the practical limitations of calling for greater net price transparency.

There are many arguing that to tackle increasing healthcare expenditure, policymakers should be looking not only to medicines, which accounts for approximately 17% (in 2018) of pharmaceutical expenditure across European markets,¹⁴² but also to inefficiencies in the system. For example, in Italy it was estimated that about 26% of the total healthcare expenditure is attributable to inefficiencies, wastages and corruption (that is, €23.6 billion in 2017, more than the double the expenditure on innovative pharmaceuticals).¹⁴³ The OECD published a comprehensive report in 2017 on approaches for tackling the wasteful spending on health amongst member states which can

140 AIFA (2020). "Decreto 10 Luglio 2020". Available at <https://www.gazzettaufficiale.it/eli/gu/2020/07/24/185/sg/pdf>

141 AIFA (2020). "Linee guida per la compilazione del Dossier a supporto della domanda di rimborsabilità e prezzo di un medicinale". Available at https://www.aifa.gov.it/documents/20142/0/AIFA_Linee+Guida_v.+16.9.2020+per+consultazione+pubblica.pdf/64f8d5b5-69df-a799-9ae7-36a5743d5f17

142 OECD (2018). "Pharmaceutical Spending, Total % of health spending". Data selected for Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, United Kingdom. Available at <https://data.oecd.org/healthres/pharmaceutical-spending.htm>

143 EURISPES (2017). "Il termometro della salute". Available at: <https://eurispes.eu/ricerca-rapporto/enpam-eurispes-il-termometro-della-salute-1-rapporto-sul-sistema-sanitario-2017/>

occur due to myriad reasons including low-value care, inappropriate medicine use, administrative spending, fraud corruption and other integrity violations.¹⁴⁴

The importance of considering the economic ramifications applies also more broadly to other debates around transparency. For instance, discussion of R&D costs transparency (which is often coupled with NPT in many policy discussions) suffers from similar issues as those highlighted for greater NPT: the political debate is not aligned with the technical implications (Table 16).

Table 16: The implications of disclosing R&D costs

Technical implications of disclosing R&D costs	
R&D cost disclosure facilitates a move away from value-based healthcare	R&D costs do not in any way reflect the value that a medicine brings to patients and society (R&D costs depend on the length of development, stringency of the approval processes, attrition rates and the cost of capital). ¹⁴⁵ While value-based healthcare and the way that it is implemented in many markets may not be the perfect medicine pricing model, its merits for innovative medicines are widely lauded.
R&D cost disclosure would undermine the efficiency of biopharmaceutical research	If R&D costs are used to inform pricing methodologies (i.e. cost-plus pricing), this would present an incentive to exaggerate costs or disincentivise productivity and likely push research towards areas of less clinical development uncertainty. ^{146,147}
Cost-plus pricing delegitimizes HTA	Shifting to cost-plus pricing to inform price negotiations would delegitimize decades of scientific developments in HTA methodologies and undermine the autonomy of national bodies in determining which medicines are best for patients.
R&D costs for a single medicine are rarely available	R&D costs for an individual medicine are considered almost impossible to calculate, especially given the costs associated with failed products and the impact that a single innovation can have across multiple medicines and disease areas.

144 OECD (2017). "Tackling Wasteful Spending on Health". Available at https://read.oecd-ilibrary.org/social-issues-migration-health/tackling-wasteful-spending-on-health_9789264266414-en#page1

145 Mestre-Ferrandiz, J., Sussex, J. and Towse, A. for The Office of Health Economics (2012). "The R&D Cost of a New Medicine".

146 Buckley, G. J., & Gostin, L. O. (Eds.). (2013). Countering the problem of falsified and substandard drugs. National Academies Press.

147 Annemans, L. (2019). "A proposal for value informed, affordable ("via") prices for innovative medicines". *Journal of medical economics*, 22(11): 1235–1239

Calculating R&D costs relevant to a single market is not possible

As a global joint cost, irrespective of the number of patients benefited worldwide, R&D investment cannot be attributed to specific countries or patients.¹⁴⁸

Although this report has not considered markets outside of Europe when discussing the potential impacts of greater NPT, the risks associated with this policy change are no doubt exacerbated when considered in this broader context. In particular, current and increasing interdependency between European and US prices could result in a significant risk to the industry innovation model and patients' access to innovative medicines today and in the future, given the share of biopharmaceutical revenue that the US is responsible for. Similarly, outside of the US, many other markets reference European prices, thereby 'raising the stakes' of greater NPT in Europe.

In summary, there is a consensus across technical experts that greater NPT is a risky and inefficient policy proposal to address issues in the healthcare system if implemented without stringent measures to mitigate against risks (e.g. prior agreement of Ramsey Pricing levels amongst participating markets). Although some advocates theorise that prices will decrease with greater NPT, economic theory has shown that the picture is significantly more complex than this, with significant associated risks for payer budgets and a danger of having the opposite impact in many markets. Only by bringing together a range of stakeholders to discuss the political and technical consequences of transparency will we be able to develop policy proposals that improve trust while maintaining efficiency in healthcare decision-making and patient access.

148

Danzon, P. M., & Towse, A. (2003). "Differential pricing for pharmaceuticals: reconciling access, R&D and patents". *International journal of health care finance and economics*, 3(3): 183–205.