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HEALTH EVIDENCE NETWORK SYNTHESIS REPORT 73

What is the evidence on legal measures to improve the transparency of markets for medicines, vaccines and other health products (World Health Assembly resolution WHA72.8)?

Katrina Perehudoff | Kaitlin Mara | Ellen 't Hoen



**World Health
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Health Evidence Network synthesis report 73

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Abstract

In 2019 the Seventy-second World Health Assembly endorsed resolution WHA72.8 to improve the transparency of markets for health products. This scoping review aims to support policy-makers in the WHO European Region who seek to develop policies related to market transparency by summarizing the current evidence on the legal implementation of measures to improve the transparency of markets for medicines, vaccines and other health products. The review identified existing mechanisms to improve the transparency of pharmaceutical markets in two main areas: (i) the price transparency of medicines, vaccines and health products and (ii) the transparency of research and development costs. It also identified two disclosure practices in individual countries that could be applied by groups of Member States: pooled procurement (by a national agency or group of payers/providers in one country) and the clearing-house method (of collecting and sharing anonymized, aggregated procurement prices for medical products). In addition, evaluations of price transparency mechanisms in upper-middle- and high-income countries in other regions provide examples of lessons learned for consideration by governments in the WHO European Region. The decision to promote greater transparency in the pharmaceutical market rests with national governments in the Region. In France and Italy, legal reforms to implement their commitments to price transparency in the pharmaceutical market are consistent with European Union law. These examples may be useful for other Member States planning to adopt laws on the provision of greater transparency.

Keywords

ACCESS TO MEDICINES, PRICE TRANSPARENCY, PHARMACEUTICAL POLICY

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ABBREVIATIONS

BPS	Banco de Preços em Saúde
EU	European Union
EURIPID	European Integrated Price Information Database (Collaboration)
MEA	managed entry agreement
MI4A	Market Information for Access to Vaccines (project)
R&D	research and development

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SUMMARY

The issue

High prices of medicines, vaccines and other health products are a justifiable cause for concern among Member States in the WHO European Region because they may limit the capacity of patients to access treatments that are critical to their care and risk overburdening limited health budgets. High prices can also create inequities within and among Member States and lead to unacceptable levels of out-of-pocket expenditure in countries of all income levels. An often-cited obstacle to addressing this problem is lack of transparency around the cost of research and development (R&D) and the prices of health products. This lack of transparency impairs the ability of Member States to make fully informed decisions when purchasing health products or negotiating the prices of health products for their populations. In recognition of this problem, the Seventy-second World Health Assembly in 2019 passed resolution WHA72.8 to improve the transparency of markets for health products. However, more insight is needed on (i) the degree to which recommendations in the resolution have been carried out by Member States in the Region and (ii) whether price transparency measures have had an impact on the prices of medicines, vaccines and other health products.

The synthesis question

To inform national and regional policies, this report synthesizes the current available evidence in the WHO European Region to address the question: “What is the evidence on legal measures to improve the transparency of markets for medicines, vaccines and other health products (World Health Assembly resolution WHA72.8)?”

Types of evidence

Evidence was obtained by a scoping review of the academic and grey literature. A total of seven academic publications and 43 grey literature publications were included in this review. A systematic survey of domestic legislation (including proposed legislation) was beyond the scope of this review.

Results

This review identified enacted European Union (EU) legislation and national legislation in France, Italy and Spain that could improve the transparency of R&D investments and costs. Online repositories of prices of medicines and medical products hosted by competent authorities were identified in 15 Member States of

the Region, in addition to the WHO database for Market Information for Access to Vaccines (MI4A) project. Only one competent authority (Icelandic Medicine Pricing and Reimbursement Committee) appears to publish the net price in its online medicines price list and one competent authority (Swiss Federal Department of Home Affairs) publishes the list price, ex-factory price and negotiated rebates on expensive, reimbursed medicines. The report also identified two disclosure practices in individual countries that could be applied by groups of Member States: pooled procurement (by a national agency or group of payers/providers in one country) and the clearing-house method (of collecting and sharing anonymized, aggregated procurement prices for medical products).

No mechanisms were identified in the WHO European Region to improve the transparency of R&D costs and better understand their relationship to price. Moreover, it was not possible to derive an exhaustive list of countries in the Region that have or have not implemented a domestic law to support pharmaceutical or medical product R&D cost or price disclosure. Therefore, case studies were selected from three countries outside the Region to provide examples of existing legislation and lessons learned for governments of the Region.

The WHO Regional Office for Europe could play a key role in supporting Member States to implement resolution WHA72.8, possibly in association with WHO collaborating centres and/or the research community. This could include creating a framework to survey the existing and proposed national legislation on medicines cost and price transparency in all Member States. A public repository of all transparency data related to medicines markets could be created to support the regular monitoring and evaluation of legislative proposals and (when adopted) their implementation in practice. To complement this, examples of best practice could be collected on which to base recommendations on which data types should be disclosed and which legal strategies should be used to achieve disclosure. Such actions could result in model legislation or a menu of legal options to aid Member States of the Region in implementing transparency measures.

In addition, the European Integrated Price Information Database (EURIPID) is an important step towards greater transparency, with the potential to support the transparency ambitions of World Health Assembly resolution WHA72.8 by acting as a clearing house to provide aggregated, anonymized net prices for medicines, vaccines and other health products. Embedding a clearing house into EURIPID could assist Member States of the Region with the selection of appropriate countries for external reference pricing and in price negotiations.

Policy considerations

In order to have transparency in markets for medicines, vaccines and other health products, it is important for Member States to ensure transparency between purchasers at national level, ensure high-cost items and items with a large budget impact are procured centrally or collaboratively in order to increase purchasing power, and engage in formal voluntary collaborations to procure medicines in multicountry groups to enable the exchange of information and assessments, as well as joint procurement.

Based on the findings of this review, the main policy considerations for Member States to improve the transparency of markets for medicines, vaccines and other health products and drive national and regional legal reform in the WHO European Region are to:

- recognize that it is within the remit of Member States to decide not to enter into confidentiality agreements with pharmaceutical manufacturers if doing so is not in the public interest;
- take steps to implement legislation at the national and regional levels that will ensure the transparency of prices (including discounts, rebates, market entry agreements and mark-ups) across the pharmaceutical supply chain, in line with WHO recommendations, recognizing that to do so is within the remit of Member States;
- adapt to multicountry contexts any existing law and policy mechanisms from specific countries for the disclosure of medicines, vaccines and health products prices and pilot these in groups of Member States (e.g. agreements may include clear terms of what could be kept confidential and what should be shared in the consultation process);
- implement price regulation and price monitoring and reporting tools and databases in a consistent manner to optimize their impact on the market;
- take steps to implement legislation to improve the transparency of R&D investments and costs, drawing from existing examples of EU and national legislation in France and Italy; and
- review national access to data about prices and costs in order to ensure informed price negotiations.



1. INTRODUCTION

1.1 Background

1.1.1 Calls by WHO for transparency about the costs and prices of medicines, vaccines and health products

Ensuring that all people have access to safe, effective, quality-assured health products¹ is essential to achieving the universal right to the highest attainable standard of health (1). However, medicine prices have risen steeply in recent years, sparking concerns from the public and health professionals alike (2). A recent economic review found that, between 2012 and 2017, 78% of the 36 top-selling branded medicines in the United States of America had increased in price by over 50% and that 44% of those 36 products had increased in price by over 200% (3). In Europe, the rising cost of medicines has led researchers to question whether health systems can bear the cost of treating patients with cancer and hepatitis C (4,5). Following a Council of the EU decision of 2016, the EU embarked upon a review of its pharmaceutical incentive mechanisms (6). At the same time, the Council also addressed the need for greater transparency by encouraging voluntary cooperation between Member States in the form of joint price negotiations between coalitions of Member States and proactive information exchange by national pricing and reimbursement agencies (6).

A cross-country comparison in 16 European countries found that ex-factory prices for the same medicine varied by 28–388% between countries (7). This finding raises the question of whether this large difference is warranted by differences in the national gross domestic product. In one example, the cost of a lung cancer treatment (pemetrexed) was €870 per unit in Greece, but €2020 per unit in Germany. Adding further complexity, the ex-factory price set by price control legislation or by manufacturers is often different from the prices paid by wholesalers, hospitals, pharmacies, patients receiving the medicine in hospitals or patients purchasing the medicine in pharmacies. These prices are likely to be arrived at through non-transparent negotiations, and price variance can lead to asymmetric access both between and within countries.

1. According to WHO, “health products include medicines, vaccines, medical devices, diagnostics, assistive products, cell- and gene-based therapies and other health technologies” (1).

A report on the pricing of cancer medicines prepared for the Seventieth World Health Assembly in May 2017 noted that many drug payers/providers now enter into managed entry agreements (MEAs; also known as risk-sharing agreements or patient access schemes) with companies to facilitate the purchase of medicines with high prices and uncertain clinical value (8). MEAs often take the form of discounts or rebates, and are nearly always confidential. This allows companies to keep list prices high for future negotiations and external reference pricing, thereby enabling them to charge the highest possible price an individual payer will tolerate (8).

In May 2019 increasing concerns expressed by Member States led to the Seventy-second World Health Assembly endorsing the *Roadmap for access to medicines, vaccines and health products 2019–2023* (9), which outlines WHO's plan of work for the period, and World Health Assembly resolution WHA72.8 to improve the transparency of markets for medicines, vaccines and other health products in an effort to expand access (1). An initial draft of resolution WHA72.8 was submitted to the World Health Assembly by a group of countries (including several European countries) seeking better standards for open reporting by all stakeholders, amidst concerns of rising prices and unequal access. The draft resolution was cosponsored by 19 countries (Andorra, Brazil, Egypt, Eswatini, Greece, India, Italy, Kenya, Luxembourg, Malaysia, Malta, Portugal, Russian Federation, Serbia, Slovenia, South Africa, Spain, Sri Lanka and Uganda) (10). In a speech at the Seventy-second World Health Assembly (11), the Portuguese Minister of Health underlined the importance of adopting a transparency resolution, by stating that

promoting transparency throughout the value chain, strengthening pricing policies, cross-sector and cross-border collaboration for information-sharing, regulation and joint procurement of medicines are paramount to enhance affordability and accessibility of medicines.

The Roadmap noted that unbiased information on health products, including on pricing, was a pressing need and an essential component of the evidence-informed decision-making that should underpin the expansion of or changes in national lists of essential medicines (12).

Resolution WHA72.8 urges the public sharing of information on the net prices of health products; results data and costs from clinical trials; sales revenue, prices, marketing costs, subsidies and incentives; and patent status information and marketing approval (1). It acknowledges the importance of differential pricing, but aimed – by encouraging data sharing – to equip Member States to (i) make



more informed decisions when purchasing health products, (ii) negotiate more affordable prices and, ultimately, (iii) expand access to health products for their populations. It requests the WHO Secretariat to support efforts towards transparency and to monitor the impact of transparency on the affordability and availability of health products, including the effect of differential pricing. A progress report will be submitted to the Seventy-fourth World Health Assembly in 2021.

1.1.2 What is a fair price and how might transparency influence it?

The tension between the need to incentivize medical innovation, which is critical for public health, and the need to ensure that health budgets can pay for health products has led to a debate over what constitutes fair pricing (13). A major challenge in determining what is fair is lack of transparency about the developmental costs associated with medicines and the prices set for finished products. WHO's working definition of a fair price is one that is affordable for both health systems and patients and, at the same time, provides sufficient market incentive for industry to invest in innovation and the production of medicines (1).

Transparency was a key agenda item at the first Fair Pricing Forum, which was cosponsored by WHO and the Dutch Ministry of Health and held in Amsterdam in 2017 (14). The Forum drew particular attention to the need for greater transparency on R&D costs, which feed into pricing decisions. At the second Fair Pricing Forum in Johannesburg in 2019, the need for greater transparency was a key consensus point, and discussions at the Forum helped to shape the draft World Health Assembly resolution (15). More recently, concerns about the need to assure universal access to new coronavirus SARS-CoV-2 (COVID-19) health technologies, in particular those in development, have promoted additional calls for cost and price transparency (16).

In order to understand how much it costs to bring a medicine to market, it is necessary to have access to cost information and the assumptions underlying the calculations (17). Estimates vary widely, with some pharmaceutical developers claiming that costs are as high as US\$ 2.6 billion and others (notably, the Drugs for Neglected Diseases initiative, a developer of non-profit-making medicines (18)) reporting a cost of only €60–190 million (US\$ 65–205 million) for the development of a new chemical entity (from which medicines and vaccines are made) (19). Even for generic medicines, for which the major cost is manufacturing, it is not always clear how prices are set. The first WHO Fair Pricing Forum in 2017 reported that government purchasers were paying many times the estimated cost of manufacture to purchase medicines (14).

1.1.3 What is meant by cost or price transparency in relation to medicines, vaccines and health product markets?

In relation to medicines markets, price transparency can mean a variety of different things, depending on context. For example, some discussions refer to transparency about the costs of R&D and clinical trials needed for the market authorization of medicines. In addition, the pricing of medicines, vaccines and health products is also complex.

All EU Member States are bound by Council Directive 89/105/EEC of 21 December 1988 relating to the transparency of medicinal product pricing (20). This Directive establishes the obligations and time frames in which national competent authorities (i.e. bodies with the delegated authority to act on this matter) must decide on the price (or price increase) of a reimbursable medicinal product. It also requires EU Member States to publish the prices of medicines in national reimbursement lists. The Directive enables national competent authorities to request detailed information from manufacturers and use a variety of criteria and methods to evaluate that data and establish price controls (Box 1).

Box 1. Council Directive 89/105/EEC, Article 2

According to Article 2 of the Directive (20), the following provisions shall apply if the marketing of a medicinal product is permitted only after the competent authorities of the Member State concerned have approved the price of the product:

3. At least once a year, the competent authorities shall publish in an appropriate publication, and communicate to the Commission, a list of the medicinal products the price of which has been fixed during the relevant period, together with the prices which may be charged for such products.

The Directive does not specify which sector(s) are concerned and in which format data should be reported. This means that different national authorities may report different types of price that are not comparable. Net prices and confidentiality agreements are not mentioned in the Directive. Moreover, confidentiality clauses in reimbursement contracts form a legal barrier to greater price transparency because they prevent European purchasers from disclosing the net prices (including discounts and rebates) they negotiate to other governments or payers/providers.



This review considered “transparency of markets” to include the cost of biomedical R&D as well as the prices at all stages of the pharmaceutical, vaccine and medical product supply chain, with a particular focus on net or procurement prices, including discounts and rebates. Greater transparency of net and procurement prices can reduce information asymmetry and support public payers/providers across the WHO European Region in price negotiations with manufacturers. The review did not consider cost or price transparency to include the prices that manufacturers provide to national competent authorities to support external reference pricing. These reported prices are unilateral and often subject to confidentiality clauses that prevent them from being shared and compared with other payers/providers. As of 2017, 29 European countries (26 out of the then 28 EU Member States, plus Iceland, Norway and Switzerland) applied external reference pricing (21). Twenty-three of these countries asked the manufacturer to supply price information from reference countries (22). An example from Germany illustrates how such price reporting works in practice. In price negotiations between the National Association of Statutory Health Insurance Funds and a pharmaceutical company, the company must provide foreign ex-factory prices from other European countries (23) or, when the actual prices cannot be disclosed, estimated actual prices. At no point do the German authorities learn the confidential prices from other countries, and all information exchanged during the negotiation remains confidential. The German authorities are unable to verify the accuracy of information they have been given. In another example, since May 2017 Austria has required by law that prices net of mandatory discounts (instead of list prices) are used in external reference pricing (24,25). These divergent national rules illustrate how the decision to promote greater transparency in the pharmaceutical market remains with Member States of the WHO European Region (and the Member States’ interpretation), rather than requirements from legislation. Moreover, there is currently no coordination of cost and/or net price transparency (inclusive of any discounts and rebates) at Regional or EU level.

1.1.4 Arguments for and against cost and price transparency

Whether full price transparency will have a net positive or net negative impact is currently the subject of debate. One of the most contentious issues is whether price transparency aids the cause of lowering prices – or raises them. On the one hand, greater price transparency would allow payers/providers to see when lower prices have been applied elsewhere and negotiate from a stronger position, thus increasing efficiencies and access; on the other hand, manufacturers might be reluctant to provide price reductions – even where they are sorely needed – in

case purchasers across all markets then ask for price reductions (26). This could have the effect of disadvantaging lower-income markets by driving the overall prices up (26,27) or of manufacturers exiting the market if the country is included in external reference pricing for larger markets.

Transparency in pharmaceutical and medical product markets is one of the central pillars of good governance and can help to improve public accountability and reduce corruption (28,29), thereby increasing public trust in the procurement system (30). Better-informed procurement processes may also lead to the optimal allocation of public resources (31). Greater transparency about the price components for medicines, vaccines and health products could provide payers/providers with the information they need to negotiate lower prices from manufacturers, and the resulting competition could lower prices further (32). Moreover, market inefficiencies resulting from information asymmetry would be reduced (8). The publication of distributor fees and mark-ups between the net price and pharmacy retail price would allow the public and policy-makers to see – and react to – these price increases. Legislation that would require greater transparency about all cost and price components would enable the public and policy-makers to identify whether price hikes are excessive.

Achieving clarity on the R&D costs can help with setting fair prices for medicines (13), and more information on sales revenues and the number of units sold could also help with determining when R&D investments have been recouped (8). In turn, these data could be used to improve the focus of research efforts, including those supported by public financing (33).

However, price transparency might reveal different prices for the same product in different markets, which could drive requests for lower prices in more-expensive markets. To avoid this, manufacturers might raise prices in the less-expensive market, leading to uniform pricing that could disadvantage low-income countries (26). Furthermore, manufacturers might collude to fix prices, particularly in smaller markets and in sectors with little competition (34). Manufacturers might also be reluctant to offer discounts to a particular buyer in case transparency about that pricing decision makes it more difficult to negotiate a higher price elsewhere (35). However, a WHO technical report for the World Health Assembly, Pricing of Cancer Medicines and its Impacts, noted that currently non-transparent medicine prices are poorly correlated with the country's ability to pay, and that many companies have already opted “not to launch or delayed the launch of medicines in countries with lower capacity to pay, irrespective of whether prices were disclosed or not” (8). A further risk is that unevenly applied transparency laws and practices – particularly



those that rely on voluntary disclosures – may worsen information asymmetries and have an unpredictable impact on medicines markets (36).

A final argument against price transparency is that any move to reduce profits could dampen industry incentives for future innovation (34) or further skew innovation towards the needs of wealthier markets (8).

1.1.5 Objectives of this report

World Health Assembly resolution WHA72.8 recommends that Member States (i) take appropriate measures to publicly share information on net prices; (ii) take steps to support access to data about the costs of clinical trials; and (iii) work collaboratively to improve the reporting of suppliers' information about sales, prices, costs, subsidies and incentives with regards to health products. The legal implementation of measures to improve transparency includes domestic and regional (e.g. EU) legislation and related mechanisms (e.g. online repositories or other cost/price data sharing practices), either with or without a legal basis in domestic law. However, no comprehensive review of the measures taken to improve medicine costs or price transparency in the WHO European Region is yet available. Therefore, this report aims to review the best available evidence to determine (i) which laws and mechanisms exist to improve the transparency of markets for medicines, vaccines and other health products and (ii) whether the implementation of these laws has improved the transparency of markets for medicines, vaccines and other health products.

1.2 Methodology

A literature search between February and July 2020 examined peer-reviewed and grey literature in English and Russian on laws or mechanisms for pharmaceutical or medical product R&D cost or price transparency in the 53 Member States of the WHO European Region, with no date restrictions. In addition, supplementary evidence from countries outside the Region was examined to provide material for policy learning. The review did not specifically seek to identify an exhaustive list of primary sources of national laws governing the transparency of research costs or of the prices of medicines, vaccines and health products.

Searches of the peer-reviewed and grey literature identified 8432 publications. After duplicate removal and title and abstract screening, 102 full-text articles were assessed, with 50 fulfilling the criteria for inclusion (22,24–27,31,37–80): seven peer-reviewed articles (26,27,31,37–39,80) and 43 grey literature articles (22,24,25,40–79). Complete details of the methodology are given in Annex 1.

2. RESULTS

The seven academic publications identified in the review comprised six observational studies (27,31,37–39,80) and one commentary (26). Of the six observational studies, four were comparative cross-sectional studies (31,38,39,80) and two were reviews of mechanisms for medicines price transparency (37) or of different pharmaceutical pricing strategies (27). The cross-sectional studies compared the characteristics of different (online) medicines price information mechanisms (38,80), procurement prices of different vaccines reported in the WHO MI4A database by procurement income group (31) and variance in the procurement price of medical products in Dutch hospitals (39). The seven academic publications were used to source laws and/or mechanisms for cost or price transparency. In addition, the review identified relevant legislation and related information from the EU (73–76) and EU Member States (24,25,60–64,81,82).

2.1 Existing laws/mechanisms to improve the transparency of pharmaceutical markets

The review identified mechanisms to improve the transparency of pharmaceutical markets in two main areas: (i) the price transparency of medicines, vaccines and health products and (ii) the transparency of R&D costs.

To enhance the price transparency of medicines, vaccines and health products, the EURIPID Collaboration (22,69–71,77), WHO (39,71,79) and national authorities in 15 Member States of the WHO European Region (40–55,78) have implemented or contributed to an online price repository of medicinal product pricing information (Table 1). However, this review did not systematically investigate whether these mechanisms have a basis in national legislation. Three mechanisms were identified to support cross-national price transparency:

- websites and other publicly accessible databases hosted by national competent authorities that voluntarily disclose one or more types of price (section 2.1.1);
- publicly accessible databases hosted by international bodies to which national agencies (or donors) can voluntarily disclose the prices they have paid and source comparator prices (section 2.1.2); and
- cooperative medicines assessment and price negotiation by multiple European countries (section 2.1.3).

Table 1. Publicly accessible online registries of price information in the WHO European Region, by country

Country	Agency	Price transparency mechanism	Type of price data
Belarus	Centre for Expertise and Testing in Health Care	State register of the maximum price of manufacturers for medicines (40)	Maximum selling price
Czechia	State Institute for Drug Control	Medicinal Products Database (41)	Maximum ex-factory price (set by law) or the ex-factory price
Denmark	Danish Medicines Agency	Medicines prices (42)	Pharmacy cost price
Estonia	State Agency of Medicines	Register of medicinal products (43)	Reference price
Iceland	Icelandic Medicines Agency	Price lists (44)	Maximum wholesale price without VAT Maximum retail price with VAT Reference price Producer discount price without VAT (no data available) Representative discount price without VAT Wholesaler discount price without VAT (no data available) Pharmacy wholesale price without VAT Reimbursement price with VAT
Italy	Italian Medicines Agency	Transparency lists (45)	Reference price (<i>prezzo di riferimento</i>) Public price (<i>prezzo al pubblico</i>)

Table 1 contd

Country	Agency	Price transparency mechanism	Type of price data
Kazakhstan	National Centre for Expertise of Medicines and Medical Devices	Price registry (46)	Maximum wholesale prices Maximum retail price
Netherlands	National Health Care Institute	Medicine cost database (47)	Average price per day (for the patient)
Norway	Norwegian Medicines Agency	List of products with maximum prices (48)	Stepped price and Reimbursed price of all medicines for humans with a maximum price ^a
Portugal	Infarmed	INFOMED human medicinal products database (49)	Public selling price with VAT (retail price; <i>preço de venda ao público</i>) Reference price Maximum price
Republic of Moldova	Agency for Medicines and Medical Devices	National catalogue of producer prices for medicines (50)	Manufacturer price (ex works)
Russian Federation	Ministry of Health	State register of maximum selling prices of manufacturers of medicines included in the list of vital and essential medicines (51)	Maximum retail manufacturer price (for essential medicines; “limiting price” in the dataset)
Sweden	The Dental and Pharmaceutical Benefits Agency	Medicines database (52)	Pharmacy wholesale price Price
Switzerland	Swiss Federal Department of Home affairs	Specialty List (53)	List price Ex-factory price Rebates

Table 1 contd

Country	Agency	Price transparency mechanism	Type of price data
Turkey	Turkish Drug and Medical Devices Agency	Reference-based drug prices lists (54)	Reference-based drug price
Multicountry agency ^b	WHO	WHO MI4A database for cross-national price comparisons ^c (31,79)	Price per dose of the vaccine purchased, and other disaggregated price components such as VAT per cent (83)

VAT: value-added tax.

^a Please note that actual prices may be lower than maximum prices stated.

^b High-income countries: Andorra, Croatia, Cyprus, Czechia, Estonia, Finland, France, Hungary, Iceland, Latvia, Lithuania, Malta, Netherlands, Poland, Portugal, San Marino, Slovakia, Slovenia, Spain and Sweden; upper-middle-income countries: Albania, Azerbaijan, Belarus, Bosnia and Herzegovina, Bulgaria, Georgia, Kazakhstan, Montenegro, North Macedonia, Romania, Russian Federation, Serbia, Turkey and Turkmenistan; lower-middle-income countries: Armenia, Kyrgyzstan, Republic of Moldova, Tajikistan, Ukraine and Uzbekistan.

^c Contributors are mostly national or subnational governments and/or health insurance agencies, but are sometimes donors.

To improve the transparency of R&D costs, France and Italy have national legislation requiring manufacturers to disclose the amount of public contributions towards these costs for medical products considered for reimbursement (section 2.1.4). The Italian decree also mandates the disclosure of the biomedical R&D costs during negotiations, and for reimbursement agreements to require the annual reporting of the sales, turnover, marketing costs and patent status of the reimbursed product in Italy. However, this review did not identify any policy mechanisms or practices (e.g. online repositories, data sharing between institutions such as hospitals) to enhance the transparency of R&D costs and public contributions in the WHO European Region.

2.1.1 National websites and other publicly accessible databases

The review found that competent authorities in 15 Member States host online price repositories and that 43 countries in the WHO European Region have implemented or contributed data to publicly accessible online price repositories (Table 1).

In Member States of the Region, competent authorities regularly publish the price lists of medicines in country-specific online databases (Table 1) (38,72). A range of price information is available on these websites, including the ex-factory price (with no distinction between list and net prices), procurement price, wholesale price (with no information on taxes and duties), reimbursement price (sometimes with no indication of whether the dispensing fee is included) and pharmacy retail price (usually with no indication of whether dispensing fees and co-payments are included). (See Annex 2 for a glossary of terms.)

At least two repositories appear to publish net medicines prices or sufficient information to calculate this. The Icelandic Medicine Pricing and Reimbursement Committee publishes the representative discount price without value-added tax in their medicines price lists, which may reflect the net price (44). The Swiss Federal Department of Home Affairs publishes the list price, ex-factory price and rebates offered on expensive medicines included on the reimbursed Specialty List (Spezialitätenliste) (53). Switzerland is one of the very few European countries to publish the rebates it negotiates on some medicines. In some cases, this information allows others to calculate the product's net price (7).

A systematic investigation of the usefulness of these 15 national databases for conducting price comparisons, and whether any of them are mandated by national or international laws, was beyond the scope of this review. Nevertheless, national legislation requiring national competent authorities to report prices on their website was identified in Armenia (reference price, maximum wholesale and retail price), Belarus (declared price), the Republic of Moldova (manufacturer price), the Russian Federation (maximum retail manufacturer price) and Tajikistan (maximum selling price) (65–68,78).

Notably, the Swiss Federal Council recently put forward legislative proposals (tabled in May 2019, amending the Federal Act of 1994 on Health Insurance (84)) which would allow pricing models (MEAs) with undisclosed discounts on expensive medicines covered by the compulsory health insurance (3). If adopted, the law would stop the publication of rebates negotiated on a growing class of expensive, reimbursed medicines, thereby preventing the accurate calculation of the net price. Furthermore, the law would prohibit the details of rebates from being obtained through a Freedom of Information request (5,6). (See Case study 1 for more information.)



Case study 1. Net price transparency in Switzerland

Switzerland has adopted World Health Assembly resolution WHA72.8 (85,86). The country particularly supported the recommendation for net price transparency, which is aligned with its general practices. The Swiss authorities maintain a publicly accessible online list of specialty (often highly priced) medicines that are reimbursed by the compulsory health insurance, along with the list price, ex-factory price and rebates offered on these products (53). Switzerland was one of few European countries to publish the rebates it negotiates on medicines. This information can allow other purchasers to calculate the product's net price (80).

However, in May 2019 the Swiss Federal Council called for the Swiss authorities to instead use pricing models (i.e. MEAs), which would not disclose the discounts on these expensive medicines, as long as other countries were using the models in order to ensure the affordability of and timely access to these medicines in Switzerland (81). In the context of cost-containment measures proposed in August 2020, the Federal Council drafted an amendment to the Federal Act of 1994 on Health Insurance (84) that would (among other policies) introduce confidential MEAs that were exempt from transparency legislation (87). If adopted, the law would prohibit the publication of the net (negotiated) price, the calculation method and negotiated rebates for a growing class of expensive, reimbursed medicines on the Specialty List (53). The law would also prohibit the details of rebates from being obtained through a Freedom of Information request (82,87). Consequently, only the list price and the ex-factory price would be made public, but rebates would become confidential, preventing calculation of the net price. The public consultation on this proposed amendment ended in November 2020 and further legislative steps have yet to be announced.

2.1.2 International publicly accessible databases

Some governments in the WHO European Region also contribute data to international price repositories. For example, WHO MI4A is a publicly accessible database to improve vaccine price transparency and support country planning, budgeting and negotiation to enhance access to vaccines (Table 1). It provides publicly available information on 590 products and their price, procurement method, volumes, sources,

presentation form and size, and other parameters (31,39). Currently, governments and national agencies in 42 Member States of the Region contribute information about procurement prices to this database (31). By 2018, 151 countries from all WHO regions and income categories had reported the 2017 prices for vaccines to the database and five countries had abstained from reporting for confidentiality reasons. Therefore, legislation and data confidentiality are barriers in only a few countries (31).

The Common European Drug Database was a multicountry repository initiated by the National Health Insurance Fund Administration of Hungary to facilitate public access to pharmaceutical prices in the EU (27,55). This database later became EURIPID, a private online portal for voluntary, non-profit-making cooperation between national competent authorities in Europe to disclose the official prices of reimbursed medicines (69,70). Its primary purpose is to aid participating authorities with external reference pricing; consequently, it does not serve as a public repository of net medicine prices as such (71). The EURIPID Collaboration has attempted to address several challenges to international price comparison, and in its second phase of funding has entered into dialogue with stakeholders and explored the inclusion of discounts (22). The European Parliament has encouraged the EURIPID Collaboration to include in its database the real prices or net prices paid by EU Member States (77).

2.1.3 Cooperative medicines assessment and price negotiation

The review found several country-led partnerships that are sharing price data, among other information, between voluntary coalitions of Member States to facilitate cooperative medicines assessment and price negotiations. Two prominent examples are the Baltic Partnership (Estonia, Latvia and Lithuania) (56) and the Beneluxa Initiative (Austria, Belgium, Ireland, Luxembourg and the Netherlands) (57–59). Within the Baltic Partnership, Estonia and Latvia jointly purchased the rotavirus vaccine in 2017 using data from the WHO M14A database (31,56). In May 2017 the Beneluxa Initiative undertook its first joint health technology assessment for Orkambi (lumacaftor/ivacaftor), a cystic fibrosis medicine. Within the context of the Initiative, two countries (Belgium and the Netherlands) entered into joint price negotiations that ended without agreement on price because the medicine was deemed not to be cost-effective (57). The Netherlands later reached a confidential price agreement with the manufacturer independently of the Initiative (Box 2 gives further details) (58).



Box 2. Price negotiations in the Netherlands

In 2017 the Dutch Minister of Health reached a price agreement with Vertex for the cystic fibrosis medicine Orkambi (lumacaftor/ivacaftor), at a cost of about €60 000 per patient per year, anticipating 750 patients per year (57,88). If the number of treatments is lower than anticipated, then the price can go up to as much as €75 000 per patient per year. Details of price deals with Vertex are normally not disclosed but, in this case, the Minister disclosed in Parliament the spending ceiling for Orkambi, which made it possible to determine the agreed price. Vertex originally asked for €170 000, so the agreed price might seem a significant discount. However, the Dutch National Health Care Institute had previously determined that this treatment would only be cost-effective at a price of around €30 000 per patient per year.

Note: in the Netherlands, the Minister was not allowed to disclose the price agreed with Vertex, but he could say what the total spending ceiling was on Orkambi (€46 million). It is possible that the confidentiality clauses did not cover the spending ceiling.

In July 2018 the medicine Spinraza (nusinersen), a treatment for spinal muscular atrophy, went through the Beluxa Initiative's joint health technology assessment procedure and a joint price negotiation with two participating countries, Belgium and the Netherlands; on this occasion, the countries reached agreement on price (59).

This review will not further explore country-led mechanisms because very little reliable information was retrieved about the type of price data exchanged within these partnerships. The WHO report on cross-country collaborations provides in-depth information about country-led partnerships (89). This descriptive analysis of five government-led, voluntary, cross-country collaborations in the WHO European Region found that in some partnerships countries had to align their national procedures and/or reform national law in order to facilitate cross-country cooperation (89).

2.1.4 Laws to support the transparency of R&D costs

No specific mechanisms to improve the transparency of R&D costs were identified in the Region. However, two European countries (France and Italy) have adopted new laws to implement their commitments to transparency in the field of medicines that aim to disclose biomedical R&D costs and the public contribution towards

these costs. These legal reforms are consistent with Member States' responsibility to manage the national pharmaceutical supply and with EU law (see Annex 3 for the text of the draft laws). In addition to these adopted laws, national laws that indirectly promote R&D cost transparency (e.g. national legislation on access to public information in Spain; Case study 2) and international laws that promote a specific goal (e.g. the EU Orphan Medicinal Products Regulation; Case study 3) can be tools to obtain information about the R&D costs of specific products.

Case study 2. Using the law on access to public information to obtain R&D costs in Spain

In 2019 the *Consejo de Transparencia y Buen Gobierno* (General Transparency Council), Spain's independent body responsible for ensuring the transparency of public activity, supported requests for the Spanish Government to publicly disclose the price of the cellular immunotherapy Kymriah (tisagenlecleucel), and the therapeutic and financial criteria used to justify its recent approval (64). This request was based on Spain's existing transparency legislation (90). This single initiative regarding one medical product will not necessarily lead to more systematic transparency in the R&D costs and prices of medicines in the future. However, it is a useful illustration of how existing laws about the transparency of government decisions can create a supportive environment for the public disclosure of medicine prices and price-setting criteria.

Case study 3. EU legislation on orphan medicinal products as a disclosure mechanism for R&D costs

EU Regulation (EC) No. 141/2000 on orphan medicinal products is a European pharmaceutical regulation that aims to create incentives to encourage pharmaceutical firms to develop medicinal products for orphan diseases (73,74). Regulation (EC) No. 141/2000 (73) states that medicinal products may receive an orphan designation if:

- the product is used for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition;
- no satisfactory method of diagnosis, prevent or treatment for the disease in question exists or, if a method does exist, then the product in question will be a significant benefit for those affected; and

Case study 3 contd

- the condition affects five or fewer patients per 10 000 population (the prevalence route) or the product is unlikely to generate a sufficient return to justify the necessary investment (the return-on-investment route).

EU legislation requires pharmaceutical firms seeking an orphan designation for a medical product based on the return-on-investment route to disclose information about their R&D costs. The specific list of information (described in EU Regulation 847/2000 on implementation) used to determine the sufficient return on investment includes data on the past and expected future developments, the production and marketing costs, details of grants and tax incentives received, and an estimate of and justification for expected future revenues (74,75).

Therefore, this regulation is one mechanism by which the R&D costs of an orphan medicine could be obtained by European regulators. However, the European Commission has so far reported only one case of a pharmaceutical company choosing to utilize the return-on-investment route between 2000 and 2015 (representing 0.04% of applications for an orphan designation) (74,76).

In 2019 the Italian Minister of Health and Minister of Economy and Finance signed a decree outlining new rules for negotiating pharmaceutical prices, which included specific reference to World Health Assembly resolution WHA72.8 in the preamble (60). In their application for reimbursement, manufacturers must submit a comparative evaluation of the candidate medicine and alternative treatments, including clinical and economic aspects (Article 2.2(a)). In the absence of comparator products, manufacturers must include economic evaluations, including a price proposal based on the costs of research, development and production (Article 3.7). All submissions must indicate the public contribution towards R&D of the candidate product (Article 2.2(g)). Reimbursement agreements should require the manufacturer to report annually to the Italian Medicines Agency the sales, turnover, marketing costs and patent status of the reimbursed medicine (Article 3.2(a)). The decree officially came into force in July 2020 (see Annex 3 for the relevant legal text).

In the second example, the French Parliament adopted an amendment to the 2021 Social Security Financing Bill on 25 November 2020 that was aligned with World Health Assembly resolution WHA72.8 (26,61). (See Annex 3 for the relevant

legal text.) The amendment is a notable first step that obliges companies to disclose in the price negotiation process the public funding contribution towards the R&D of new medicinal products (61,62). According to a subamendment, the disclosure is a total amount; it is not specific to the medicinal product for which the price is being negotiated (Pauline Londeix, personal communication, 2021). The disclosures would be made public and taken into consideration by the *Comité économique des produits de santé* (Economic Committee for Health Products), which is responsible for price negotiations (63). These rules will be further clarified and implemented in a decree to be adopted by the French Government at some point in the future (63).


Beyond these examples, a systematic study of national legislation in the WHO European Region is required to provide a complete overview of the existing laws supporting greater transparency of R&D costs.

2.2 Impact of laws/mechanisms on the transparency of pharmaceutical markets

A previous scoping review identified no robust research on the implementation of intercountry pharmaceutical cost or price transparency laws and mechanisms in the WHO European Region (37). However, other national disclosure laws or practices can indirectly be used to promote cross-country transparency in medical product markets.

Similarly, this review found no evidence of implementation of laws that directly promote R&D cost and price transparency for pharmaceutical products across the WHO European Region. However, existing laws and mechanisms were identified that influence the transparency of pharmaceutical markets: national disclosure laws or practices can be indirectly used to promote cross-country transparency in medical product markets (section 2.2.1), whereas confidential discounts and rebates can impair price negotiations (section 2.2.2).

In addition, evaluations of existing price transparency mechanisms from upper-middle- and high-income countries in South America can provide policy lessons for Member States of the WHO European Region (Case study 4). A large number of middle-income countries in the Region have gross domestic products that closely resemble those of some South American countries. Moreover, experiences of pharmaceutical procurement in the national health service of Brazil provide insights for Member States with nationalized health services, such as the United Kingdom. However, the limitations of such comparisons should also be recognized.



For example, confidential discounts and rebates, and MEAs in general, are more common in high-income countries; therefore, most South American countries are unlikely to provide insight into these areas.

Case study 4. The South American experience: transparency for price comparison and public accountability

In an effort to reduce medicine prices and centralize such information, the Brazilian Federal Government adopted legislation in 1998 that established the *Banco de Preços em Saúde* (BPS; Health Price Database) (91,92). BPS was initially implemented to collect and publish the purchase prices of medical supplies and related information from all federally funded hospitals with 320 beds or more, but it is now a publicly accessible repository of such purchase prices from all public and private institutions registered in the system (91). In 2017 disclosure and use of the BPS became mandatory for all municipalities, states and the Federal District, with private institutions providing purchasing information on a voluntary basis (91). BPS is used to manage the supply and demand of medical products, monitor price trends and increase supplier access to payers/providers, inform public decisions through price comparison, and enhance transparency and social control over public health resources (via public access to the online database) (91,93). Information provided by the BPS repository includes the quantity, unit price, percentage compared with the lowest price, brand, form of bidding, country of purchase, purchase receipt number, number of bids, the vendor's name, and the manufacturer's name and country.

However, the effect of the BPS tool on pharmaceutical prices has been little studied. A review of some essential medicines found that the existence of the BPS did not result in consistent reductions in purchase prices (91). This comparison of two Brazilian states found a decrease in the unit price for five of the 19 medicines studied in the state with lower socioeconomic status (Paraíba) over an eight-year period (2005–2013); however, these decreases were not seen in the state with the higher socioeconomic status (São Paulo). The launch in 2004 of *Farmácia Popular*, a major pharmaceutical provision programme for low-income households, was suggested to have influenced the supply and demand of medicines in the study.

Another South American country also has medicine price transparency initiatives with a legal basis. Chile, a high-income country, introduced the ChileCompra e-procurement system in 2010 to centralize and digitize the

Case study 4 contd

negotiation of multiyear agreements with suppliers (91). This measure stemmed from implementation of the 2003 Law on Procurement and complementary regulations on public procurement processes (91).


The Brazilian example suggests that the government did not take regulatory action on the price increases revealed by the databases and surveys (91). Therefore, price monitoring and reporting tools may only be effective in exerting downward pressure on prices when regulation and enforcement are consistently practised.

2.2.1 Disclosure practices improve transparency within countries

Two intracountry disclosure practices or policies and evidence of their impact were identified in three WHO European Member States. These practices can indirectly support intercountry price disclosure and comparison among several Member States. Where known, the legal basis for these practices is reported below.

The first policy is centralized (or pooled) procurement by the Danish agency Amgros (the legal basis is the Danish law on public procurement (Law no. 1564 of 15 December 2015) (94) and EU Directive 2004/18/EC on public procurement) (95). Pooled procurement refers to the formal process of purchasing products through a central body that collects the orders from and acts on behalf of multiple payers (i.e. contracting authorities). Pooled procurement may be done through tender, which allows the central body to choose the best offer (i.e. the lowest price for the desired product characteristics). The national agency serves five Danish regions, where it buys pharmaceuticals for all public hospitals using different tendering strategies depending on the patent status of the medicine (24). In 2015 Amgros reportedly saved an estimated €314 million through centralized procurement.

The second example is the clearing-house approach, in which a third party collects data that can include discounted/net prices from purchasers and shares this aggregated, anonymized information with the other participating purchasers (24). This mechanism is thought to enhance price transparency within the limitations of existing confidential price negotiations. A clearing-house approach has been proposed as part of the health-care reform in Austria (24). In the Netherlands, the Hospital Purchase Benchmark clearing-house system was introduced as a



private initiative to compare the prices of medical products at different hospitals (with each responsible for purchasing these products) (38). By granting hospitals access to the benchmark data in exchange for providing information about their purchase orders, the clearing house secures involvement from purchasers, reduces information asymmetry and strengthens the bargaining position of purchasers (38). In 2017 data from the Hospital Purchase Benchmark revealed large price variations for 17 commonly used medical products (e.g. pacemakers, gloves and stents) in 38 Dutch hospitals (38).

2.2.2 Confidential discounts and rebates impair price negotiations

Although standard practice in many Members States of the WHO European Region, the use of discounts and rebates as forms of price reduction is an important barrier to implementing the medicines price transparency component of World Health Assembly resolution WHA72.8 (23,37). In 2011 eight Members States of the WHO European Region (Belgium, Germany, Greece, Hungary, Italy, Portugal, Spain and Turkey) reported that they have laws or regulations stipulating the level of price reductions or refunds (96). Some governments, such as the Spanish Government, have used confidential discounts (instead of transparent price reductions) as a method to reduce costs in the global financial crisis (97). However, these discounts can lead to discrepancies between the list (i.e. ex-factory) price and actual (i.e. net) price of medicines, and can impair accurate international price comparisons (which use non-discounted prices) (96,97).

The pharmaceutical industry plays a central role in keeping price negotiations and agreements confidential and inaccessible to both European purchasers and researchers. Policy-makers in several EU Member States have highlighted information asymmetry as a major challenge in pharmaceutical price negotiations with manufacturers (98). Manufacturers have knowledge about the discounts and rebates offered to all other European purchasers, giving the pharmaceutical industry an advantage in negotiations (98). Moreover, confidentiality clauses in reimbursement contracts form a legal barrier to greater price transparency because they prevent European purchasers from disclosing the discounts and rebates they receive to other governments or purchasers.

Research on actual or net medicine prices is lacking (99) and studies can be hampered by the confidential nature of medicine prices, discounts and rebates. For example, the pharmaceutical industry threatened to take legal action against the Belgian Health Care Knowledge Centre during its 2017 investigation into the terms of MEAs (using exact amounts or percentages of discounts, which would be

reported as aggregated, anonymous amounts) (100). Consequently, the researchers stopped the collaboration with industry and instead based their analysis on publicly available information (100). These reports are consistent with the broader trend of pharmaceutical industry lobbying and influence in EU public policy (101).

One study identified two main strategies to respond to rebates and discount agreements that can impair international price comparisons (98). First, it found that the inclusion of clear terms in the reimbursement contracts governing these agreements is needed to facilitate price transparency. A reimbursement contract includes agreements whereby a manufacturer will pay a public payer an (annual) rebate related to the retail cost, volume of use or other measure of the medicine purchased (98). These contracts often require that the prices provided by the manufacturer are kept confidential. However, important exceptions were found; for example, reimbursement contracts in the United Kingdom allow the information to be provided to competing manufacturers (37,98,102). Secondly, the study recommended reasonable transparency (defined as disclosure of the existence, purpose and type of reimbursement contracts in place), which, it argued, is required for payer accountability and legitimacy (98). The study found that in countries where reimbursement contracts are well established, these governments have clear standards for contract proposal and explicit policies about what is considered confidential and what should be shared in consultation processes. Having clear standards of what will be disclosed may prevent conflicts down the line and provides useful information to competing manufacturers in a way that does not disclose final prices to other payers.



3. DISCUSSION

3.1 Strengths and limitations of this review

A strength of this scoping review on laws and mechanisms for market transparency of medicines, vaccines and other health products is that it considered academic and grey literature in English and Russian, with the possibility to screen any articles identified in Dutch and French, with no time limitations on implemented cost/price transparency measures. Despite this, a key limitation was the lack of available data: of the 8432 publications screened, only 50 were relevant to the review question. Publications were excluded because they did not concern laws or mechanisms for cost/price transparency or the role of (national) governments in cost/price transparency, or because they were not based in the WHO European Region. However, the scarcity of publications about national legislation for cost/price transparency, together with the fact that only five articles on high-income countries in the Region were identified, limits the generalization of the review findings. It is also possible that information about the legal implementation of medicines price transparency measures published in languages other than English and Russian was missed. Moreover, the domestic laws and mechanisms included in the review may not reflect the latest legal developments. However, most of the identified publications could be utilized to identify relevant cost/price transparency legislation and/or mechanisms (e.g. online repositories and clearing-house strategies).

A 2020 review of the global literature on domestic mechanisms for medicines price transparency also included evidence of their effect (37). Although that review is assumed to have only considered articles in English, its findings corroborate those of the present review, which has a narrower geographical base but wider language base. Notably, there is nascent empirical evidence from the multiple country-led partnerships to improve access to medicines and vaccines, even though some of these partnerships have been progressively initiated since 2012 (89). However, even several years after their initiation, little can be said about the effectiveness of these partnerships in achieving price transparency. In order to understand the impact of these initiatives, key performance indicators may be required.

Two main reasons may account for the lack of data on medicines cost and price transparency. First, manufacturers and some governments seek to keep pharmaceutical prices confidential, making it difficult to find published information. Governments may have signed non-disclosure agreements with manufacturers and/or governments, and may believe they have already negotiated an optimal price

that must be kept secret in order to be retained. Secondly, World Health Assembly resolution WHA72.8 had only been in place for one year at the time of the literature searches. Therefore, it may be too soon after endorsement of the resolution for enough legislative action to have been taken to enable a comprehensive review or for the publication of a rigorous study of those actions. However, recent laws in France and Italy indicate that this scoping review has been particularly timely for revealing current debates and legal reforms.

Another limitation is that no formal quality and risk of bias assessments were possible because the small number of studies included were descriptive and heterogeneous in their scope and design.

3.2 Improving the transparency of pharmaceutical markets

World Health Assembly resolution WHA72.8 emphasizes that medicines R&D costs and prices are global issues with a profound impact on health budgets, and that transparency about how those costs and prices are calculated is increasingly important. This review identified various legal and regulatory mechanisms that have been used in the WHO European Region and beyond to achieve disclosure (Table 2). These mechanisms include legislation and regulations on reporting and on pricing and reimbursement (and pooled procurement legislation), as well as laws that are not directly relevant to medicine pricing but can impact price transparency, such as access to public information laws. In addition to existing EU legislation, the review found that several Member States of the WHO European Region have subsequently proposed domestic legislation and/or mechanisms to support greater cost and price transparency. These mechanisms have been implemented to varying extents by the Member States. Legal reforms that have been adopted in France and others that have come into force in Italy (in 2020, when this report was being developed) would require manufacturers to disclose the public contribution towards R&D costs of new medicinal products as part of the reimbursement evaluation. Italy's decree also requires that the costs of biomedical R&D be disclosed in the reimbursement negotiation, and that the reimbursement agreement requires the manufacturer to report annually the sales, turnover, marketing costs and patent status of the reimbursed medicine to the Italian Medicines Agency. Online repositories of medicines and medical product prices hosted by competent authorities were identified in 15 WHO European Member States, plus one hosted by WHO (MI4A database (59)).

Table 2. Legal measures to promote transparency of pricing and R&D costs

Mechanism type	Country (relevant section of this report)	Details
Reporting prices	Armenia (reference price, maximum wholesale and retail price) (65), Belarus (declared price) (66), Russian Federation (maximum retail manufacturer price) (68) (section 2.1.1)	National legislation requiring national authorities to report prices
Reporting purchasing information	Brazil (92) (Case study 4)	National legislation establishing the BPS, which requires the disclosure of purchase prices of medical supplies and related information for all municipalities, states and the Federal District, with private institutions providing purchasing information on a voluntary basis
Pricing and reimbursement negotiation	France (63) (Annex 3)	National legislation requiring companies to disclose public funding contribution towards the R&D of new medicinal products during negotiations of the prices to be covered by social security
Pricing and reimbursement negotiation	Italy (60) (Annex 3)	National legislation requiring manufacturers to disclose information about costs of research, development and production, and the public contribution towards R&D, during reimbursement and price negotiations, as well as annual reporting about sales, turnover, marketing costs and patent status of the reimbursed medicine, to the Italian Medicines Agency

Table 2 contd

Mechanism type	Country (relevant section of this report)	Details
Access to public information legislation	Spain (90) (Case study 2)	National legislation requiring transparency in Government decisions and effectuating citizens' right of access to public information. Unlike other legal measures in this table, disclosure is not automatic and relies on citizens requesting that the information be disclosed
Orphan medicine designation	EU Regulation (EC) No. 141/2000 on orphan medicinal products (73) (Case study 3)	EU legislation requires pharmaceutical firms seeking an orphan designation for a medical product based on the return-on-investment route to disclose data on past and expected future developments, the production and marketing costs, details of grants and tax incentives received, and an estimate of and justification for expected future revenues
EU reporting requirements	EU Council Directive 89/105/EEC 1988 on the transparency of medicinal product pricing (20) (section 1.1.3)	EU legislation requiring Member States to publish the prices of medicines in national reimbursement lists

For EU Member States, Council Directive 89/105/EEC of 21 December 1988 mandates competent authorities to publish, at least annually, “a list of the medicinal products the price of which has been fixed during the relevant period, together with the prices which may be charged for such products” (20). However, the Directive does not specifically require the publication of net prices.

However, only one competent authority, the Icelandic Medicine Pricing and Reimbursement Committee, appeared to publish the net price in its online medicines price lists (44). In addition, the Swiss Federal Department of Home Affairs publishes the list prices, ex-factory prices and negotiated rebates in its online database of expensive medicines on the Specialty List (53). This information makes it possible to calculate the net price in some cases. Recent legislative proposals aim to make



these rebates confidential and not subject to Freedom of Information requests. Disclosure practices in specific countries that could be applied between WHO European Member States include pooled procurement (by a national agency or group of purchasers in one country) and the clearing-house method of collecting and sharing aggregated, anonymized procurement prices for health products.

No robust research was identified on the implementation of R&D cost or price transparency laws or mechanisms in the Region, probably because of insufficient time since adoption of the resolution for domestic legal reforms to emerge. Nevertheless, studies of price transparency legislation and mechanisms from upper-middle- and high-income countries were identified in other world regions to provide examples of lessons learned for European governments (Table 2).

3.2.1 A need for further research

No mechanisms were identified in the WHO European Region to improve the transparency of R&D costs. Based on the published literature, it was not possible to derive a complete list of countries in the Region that have or have not implemented a domestic law to support cost or price disclosure. Therefore, a systematic survey of domestic legislation and draft legislation would be an important step towards elucidating the real-time legal provisions on medicines price transparency in the WHO European Region, but this was beyond the scope of this review. High-quality prospective studies of the effect of laws promoting cost or price transparency measures in the Region are also needed as these laws become adopted and implemented. Such studies require a robust definition of medicines cost/price transparency and stringent methods for assessment. If researchers are involved in the planning, adoption, implementation and/or evaluation of legal initiatives for price transparency, then the evidence base can be expected to grow over the next few years.

3.2.2 Actions at the global and regional levels

WHO is still in the early stages of implementing World Health Assembly resolution WHA72.8. In 2020 it updated the *WHO Guideline on country pharmaceutical pricing policies* (which includes transparency policies) (103). In addition, WHO is convening a working group to explore pricing systems that will be sensitive to the ability of health systems to pay, and is developing a framework to analyse the available research on the impact of cost or price transparency, especially for small markets and low- and middle-income countries. A third Fair Pricing Forum took place in 2021.

The European Commission's Pharmaceutical Strategy for Europe for 2021–2024 identified transparent R&D costs and agreed pricing principles as important

foundations for policy debates on pharmaceutical pricing (104). Establishing new ways of sharing information about new pharmaceuticals across countries is a priority area to complement cross-country collaborations for joint medicines pricing and reimbursement negotiations. Therefore, in the next four years the European Commission plans to engage with Member States of the EU to develop non-legislative guidelines on principles and costing methods for establishing the R&D costs of medicines. In addition, the Commission plans to support cooperation between the competent authorities of EU Member States to share best practices on pharmaceutical pricing and procurement.

WHO European Region Member States in eastern Europe and central Asia include the five members of the Eurasian Economic Union (i.e. Armenia, Belarus, Kazakhstan, Kyrgyzstan and the Russian Federation) (105). Therefore, the Eurasian Economic Commission (106) could consider supporting collaboration between these countries to implement measures related to World Health Assembly resolution WHA72.8 and managing the market. The WHO Regional Office for Europe can play an important role in supporting Member States of the Region to enhance the transparency of medicines, vaccines and medical product markets through a number of actions. First, together with WHO collaborating centres and/or the research community, it could create a framework to survey the existing and proposed national legislation of all Member States. This framework would support systematic research on the existing laws supporting medicines cost and price transparency. Secondly, the Regional Office could work with partners to establish a public repository of all transparency data related to medicines markets, from the cost of R&D to the final retail prices at pharmacies. Such a repository would support the regular monitoring and evaluation of legislative proposals and (when adopted) their implementation in practice. Thirdly, regional legislation, such as EU legislation, can also influence government and supplier actions on medicines cost/price transparency. Therefore, WHO could assess EU and other regional legislative mechanisms that can support cost/price transparency to identify best practice and share examples with other policy-makers across WHO regions. Finally, WHO could provide recommendations on which data types should be disclosed (e.g. drug registration, research costs and pricing components) and the legal strategies used to achieve disclosure (i.e. access to public information laws, pricing and reimbursement regulations or pooled procurement legislation). These recommendations could result in model legislation drawn from regional best practices (Annex 3 shows some preliminary examples) or a menu of legal options to aid Member States of the Region in implementing transparency measures. This work could be undertaken in conjunction with the key actions planned in the European Commission's 2021–2024 Pharmaceutical Strategy for Europe (104).



The EURIPID Collaboration represents an important step towards greater transparency, with the scope and potential to support the transparency ambitions of resolution WHA72.8. The Collaboration could aid participating authorities with external reference pricing and price negotiations by exploring strategies to act as a clearing house to provide aggregated, anonymous net prices of medicines, vaccines and health products (71).

3.2.3 Actions by Member States

Optimal price negotiations require that all parties should be fully informed of the prices that other purchasers pay. To reach this point, Member States of the WHO European Region would need to refuse to enter into non-disclosure agreements with pharmaceutical manufacturers. It also requires the disclosure of any discounts and rebates applied in the pharmaceutical supply chain, in line with the WHO Guideline on country pharmaceutical pricing policies (103) and World Health Assembly resolution WHA72.8 (1). In the meantime, the reforms in France and Italy illustrate how to create a supportive environment for cost/price transparency. Each new agreement between a Member State and pharmaceutical manufacturer can be considered on a case-by-case basis as a separate and new opportunity to consider whether it is in the public interest to disclose prices, discounts and rebates.

In addition, Member States could voluntarily collaborate in groups to procure medicines to overcome the limitations of country-specific negotiations (shown in Box 1). Therefore, Member States could improve their negotiating positions by voluntarily sharing prices with each other, negotiating collectively and consolidating demand. A recent WHO report on cross-country collaborations offers insight into the successes and challenges of these initiatives to date (89).

3.3 Policy considerations

Based on the findings of this review, the main policy considerations for Member States to improve the transparency of markets for medicines, vaccines and health products and drive national and regional legal reform in the WHO European Region are to:

- recognize that it is within the remit of Member States to decide not to enter into confidentiality agreements with pharmaceutical manufacturers if doing so is not in the public interest;

- take steps to implement legislation at the national and regional levels that will ensure the transparency of prices (including discounts, rebates, market entry agreements and mark-ups) across the pharmaceutical supply chain, in line with WHO recommendations, recognizing that to do so is within the remit of Member States;
- adapt to multicountry contexts any existing law and policy mechanisms from specific countries for the disclosure of medicines, vaccines and health products prices and pilot these in groups of Member States (e.g. agreements may include clear terms of what could be kept confidential and what should be shared in the consultation process);
- implement price regulation and price monitoring and reporting tools and databases in a consistent manner to optimize their impact on the market;
- take steps to implement legislation to improve the transparency of R&D investments and costs, drawing from existing examples of EU and national legislation in France and Italy; and
- review national access to data about prices and costs in order to ensure informed price negotiations.



4. CONCLUSIONS

Despite the limited availability of evidence on the legal implementation of medicines cost and price transparency, this review has revealed where these measures are currently used and offers useful directions for future research, policy and practice. The patchwork of legislation for transparency across Member States points to a key conclusion of this review: creating greater transparency in the pharmaceutical market is a political decision that rests with Member States. The new legal requirements in France and Italy show that it is within the remit of governments of Member States of the Region and consistent with EU law to enact legislation requiring greater cost/price transparency from manufacturers. Engaging in non-disclosure agreements with pharmaceutical manufacturers is contrary to the principles of good governance, the central pillars of which are transparency and accountability, and to WHO recommendations for Member States to publicly share information on the net prices of health products (i.e. after subtracting the value of discounts and rebates) and work collaboratively to improve the reporting of information such as prices, marketing costs and subsidies by suppliers of medicines, vaccines and health products.

Although it has not been possible to draw strong conclusions from this scoping review, the South American example suggests that cost or price transparency alone is unlikely to guarantee a reduction in medicine prices or expanded access to medicines. Member States will have differing abilities to pay and make different choices over spending priorities. Additional measures, for example tiered pricing, and further regulation will be required to address other issues. It will also be important for Member States of the WHO European Region to determine the best way to operationalize and utilize the cost/price data in order to maximize affordable access to essential health products.


WHO and Member States of the Region should continue exploring other mechanisms to meet these challenges, including ensuring that transparency initiatives are coupled with adequately resourced monitoring and enforcement initiatives.

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ANNEX 1. SEARCH STRATEGY

Databases and websites

Searches of peer-reviewed literature in three English-language databases (HeinOnline, Ovid MEDLINE and Scopus) were carried out between 21 February and 18 April 2020 and in two Russian-language databases (Scientific Archive of the Russian Federation and e-library.ru) on 18 March and 4 April 2020, respectively.

A structured Google Scholar search in English and Russian and searches of grey literature in the following websites were performed between 21 February and 18 April 2020: the Commonwealth of Independent States legal acts database (in Russian) (1), the EU Alliance for Innovation and Access email listserv (in English) (2) and Knowledge Ecology International (3). These were supplemented by manual searches of Eurasian Economic Commission (in Russian) (4) and all available websites of the country-led partnerships, Beneluxa Initiative (5) and the Visegrad Group (in English) (6). In addition, as recommended by the reviewers, a search of WHO Medicine price information sources (7) was conducted between 22 June and 3 July 2020.

Table A1.1 shows search terms and synonyms in English and Russian.

Table A1.1. Search terms and synonyms

English	Russian
transparency price medicines	прозрачность цен лекарств
medicine price transparency	лекарства цены прозрачность
medicine transparency	лекарства прозрачность
medicine price	лекарств* и цен*
medicines and transparency	лекарств* и транспарентность
pharmaceutical and price	фармацевтические препараты и цен*
transparency of pharmaceutical market	прозрачность рынка лекарственных препаратов

Table A1.1 contd

English	Russian
joint purchasing	совместные закупки
medicines joint purchasing	совместные закупки лекарства
parallel import medicines	параллельный импорт лекарств
research development medicines price	исследования разработка лекарств цена
medicine price transparency	лекарств* и цен* и прозрачн*
medicine and price transparency	лекарств* и транспарентность цен
pharmaceutical and transparency price	фармацевтические препараты и транспарентность
transparency	транспарентность, прозрачность
transparency expenses medicines	затрат лекарства
transparency of prices of medicines	прозрачность цен* лекарств*
medicines pooled procurement	объединенные закупки лекарства

Study selection

Duplicates were removed from the list of search results in databases with this functionality (Ovid MEDLINE and Scopus), followed by title/abstract screening against the inclusion and exclusion criteria, and full-text screening to confirm eligibility. Other relevant articles were obtained based on reviewer recommendations and snowball searching of the references in eligible studies.

Articles were included if they were:

- published in Dutch, English, French or Russian;
- based on a population or jurisdiction that was a Member State of the WHO European Region;

- focused on pharmaceutical products or devices, specifically those financed in part or wholly by domestic governments; and
- the intervention of interest was a regional or domestic law or mechanism through which a government discloses or shares medicine or vaccine R&D costs or prices.

Articles were excluded if they were:

- reports of any laws, policies, data or mechanisms for price transparency that were not governed or implemented by national governments/agencies in the Region, such as:
 - reports in which manufacturers voluntarily declare their prices;
 - surveys in which independent researchers submit reports of data collected through facility surveys;
 - sources that include information from suppliers and payers/providers outside the Region; and
 - paid services.

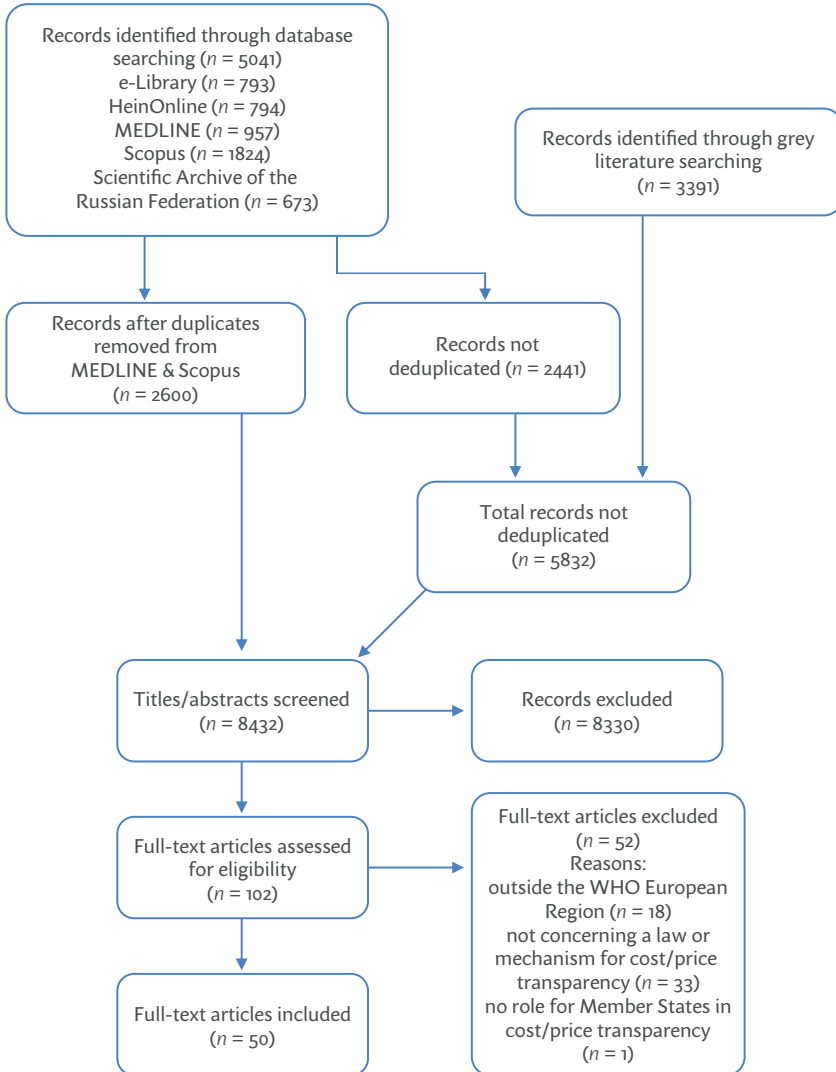
Screening and data collection

Publication details of the search results in English were imported into Mendeley and deduplicated (using the deduplicate function). The list of deduplicated publication details was then imported into Rayyan (semi-automated mechanism for initial screening of abstracts and titles). Screening was unblinded and conducted by two researchers. Peer-reviewed literature in Russian was screened by a Russian-speaking collaborator in consultation with another author.

The initial search identified 8612 publications. After duplicate removal, 8432 publications were included in the study for screening based on title and abstract; 102 publications were screened for full text and a final group of seven academic publications and 43 grey literature publications were included in the review (Fig. A1.1).

Most of the 50 publications included in this review were utilized to map, locate and understand the characteristics of relevant cost/price transparency legislation and/or mechanisms. Data extracted included the author, year of publication and country of implementation; any relevant legislation and/or websites; study design; data sources; and outcome measures.

Fig. A1.1. Selection of studies



Search terms: database searches

Search terms were derived from the three concepts guiding the search and tailored to the precision of each database (Table A1.2).

Table A1.2. Search blocks and search terms

Search block	Search terms
Pharmaceutical	medicine; pharmaceutical; drug; medication; vaccine; Drugs, Essential [MeSH]; Prescription Drugs [MeSH]
Price transparency and implications	
Sub-block 1: price transparency	price transparency; price sharing; share price*; price level*; published price*; price negotiation*; negotiating price*; negotiated price*; price disclosure*; price regulation*; regulate price*; confidential price*; price information; price comparison*; price data*
Sub-block 2: joint purchasing	joint purchas*; pooled procurement; pool procurement
Sub-block 3: parallel trade	parallel trade; parallel import; parallel export
Sub-block 4: R&D costs	innovation spending; innovation expenditure; innovation costs; research and/& development spending; research and/& development expenditure; research and/& development costs; R&D spending; R&D expenditure; R&D costs
Member States of the WHO European Region	Albania; Andorra; Armenia; Austria; Azerbaijan; Belarus; Belgium; Bosnia; Bulgaria; Croatia; Cyprus; Czechia; Czech Republic; Denmark; Estonia; Finland; France; Georgia; Germany; Greece; Herzegovina; Hungary; Iceland; Ireland; Israel; Italy; Kazakhstan; Kyrgyzstan; Latvia; Lithuania; Luxembourg; Malta; Moldova; Monaco; Montenegro; Netherlands; Macedonia; Norway; Poland; Portugal; Romania; Russian Federation; the Russian Federation; San Marino; Serbia; Slovakia; Slovenia; Spain; Sweden; Switzerland; Tajikistan; Turkey; Turkmenistan; Ukraine; United Kingdom; Great Britain; Uzbekistan

Ovid MEDLINE

The following search terms were used for advanced searches in Ovid (Medline): Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE Daily and Ovid MEDLINE <1946-Present>.

ID	Query	Number of hits
1	price transparency.tw,ti,ab.	170
2	price sharing.tw,ti,ab.	3
3	share price*.tw,ti,ab.	46
4	price level*.tw,ti,ab.	220
5	published price*.tw,ti,ab.	23
6	price negotiation*.tw,ti,ab.	143
7	negotiating price*.tw,ti,ab.	17
8	negotiated price*.tw,ti,ab.	54
9	price disclosure*.tw,ti,ab.	20
10	price regulation*.tw,ti,ab.	161
11	regulate price*.tw,ti,ab.	7
12	confidential price*.tw,ti,ab.	12
13	price comparison*.tw,ti,ab.	85
14	price data*.tw,ti,ab.	213
15	price information.tw,ti,ab.	106
16	joint purchas*.tw,ti,ab.	27
17	collective purchas*.tw,ti,ab.	14
18	pooled procurement.tw,ti,ab.	23
19	pool procurement.tw,ti,ab.	1

ID	Query	Number of hits
20	parallel trade.tw,ti,ab.	42
21	parallel import.tw,ti,ab.	22
22	parallel export.tw,ti,ab.	2
23	((research and development) adj3 (spending or expenditure or costs)).tw,ti,ab.	1956
24	(innovation adj3 (spending or expenditure or costs)).tw,ti,ab.	93
25	(research & development adj3 (spending or expenditure or costs)).tw,ti,ab.	8
26	(R*D adj3 (spending or expenditure or costs)).tw,ti,ab.	21 149
27	(pharmaceutical* or drug* or medicine* or medication* or vaccine*).tw,ti,ab.	2 453 344
28	(Albania or Andorra or Armenia or Austria or Azerbaijan or Belarus or Belgium or Bosnia or Herzegovina or Bulgaria or Croatia or Cyprus or Czechia or Czech Republic or Denmark or Estonia or Finland or France or Georgia or Germany or Greece or Hungary or Iceland or Ireland or Israel or Italy or Kazakhstan or Kyrgyzstan or Latvia or Lithuania or Luxembourg or Malta or Monaco or Montenegro or Netherlands or Macedonia or Norway or Poland or Portugal or Moldova or Romania or Russian Federation or the Russian Federation or San Marino or Serbia or Slovakia or Slovenia or Spain or Sweden or Switzerland or Tajikistan or Turkey or Turkmenistan or Ukraine or United Kingdom or Great Britain or Uzbekistan).ti,ab,tw.	639 092
29	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26	24 239
30	27 and 29	6404
31	28 and 30	957

Scopus

ID	Query	Number of hits
1	TITLE-ABS-KEY (medicine OR pharmaceutical OR drug) AND TITLE-ABS-KEY (price) AND TITLE-ABS (transparency OR disclosure OR sharing)	578
2	TITLE-ABS-KEY (medicine OR pharmaceutical OR drug) AND (TITLE-ABS-KEY (parallel trade) OR TITLE-ABS (parallel import) OR TITLE-ABS (parallel export))	630
3	TITLE-ABS-KEY (transparency OR disclosure OR sharing) AND TITLE-ABS-KEY (medicine OR pharmaceutical OR drug) AND (TITLE-ABS-KEY (research AND development) AND TITLE-ABS-KEY (spending OR expenditure OR costs))	416
4	TITLE-ABS-KEY (medicine OR pharmaceutical OR drug) AND (TITLE-ABS (transparency OR disclosure OR sharing) AND (TITLE-ABS-KEY (innovation) AND TITLE-ABS-KEY (spending OR expenditure OR costs)))	200

HeinOnline

(medicine or pharmaceutical or drug) AND (((price) AND (transparency or disclosure or sharing)) OR ((transparency or disclosure or sharing) AND (research OR development OR innovation) AND (spending OR expenditure OR costs)))

Number of hits: 794

e-Library

ID	Query	Number of hits
1	лекарств* и цен*	279
2	лекарств* и транспарентность	1
3	фармацевтические препараты и цен*	275
4	прозрачность рынка лекарственных препаратов	8
5	совместные закупки	211

ID	Query	Number of hits
6	совместные закупки лекарства	2
7	параллельный импорт лекарств	3
8	исследования разработка лекарств цена	14

The following search terms yielded no results: лекарств* и цен* и прозрачн*; лекарств* и прозрачность цен; фармацевтические препараты и прозрачность; прозрачность затрат лекарства; прозрачность цен* лекарств*; объединенные закупки лекарства.

Scientific Archive of the Russian Federation

The Boolean operators AND, OR and NOT are not functional in this database. Consequently, three-word phrases can yield 180 000–200 000 results. The only way to further specify or filter search results is to order them by rank (highest, high, medium, conditional, low). Selecting the top three ranks (which include doctoral theses and journal articles) for one-word phrases often results in around 200 000 hits. Therefore, the following search strategy was used to narrow the results.

ID	Query	Number of hits
1	лекарства цены прозрачность	73 highest and high ranked documents
2	лекарства цены прозрачность	First 200 medium-ranked documents
3	совместные закупки лекарства	First 200 of the highest-, high- and medium-ranked documents
4	параллельный импорт лекарств	First 200 of the highest-, high- and medium-ranked documents

Search terms: website searches

Google Scholar

ID	Query	Top hits screened
In English		
1	(law, policy, drug, vaccine, Europe) + (parallel trade)	100
2	(law, policy, drug, vaccine, Europe) + (research development innovation)	100
3	(law, policy, drug, vaccine, Europe) + price transparency, sharing)	100
4	(law, policy, drug, vaccine, Europe) + (pooled procurement joint purchasing)	100
5	(Baltic Partnership) + pharmaceuticals	40
6	(Beneluxa Collaboration) + pharmaceuticals	40
7	(FINOSE collaboration ²) + pharmaceuticals	40
8	(Nordic Pharmaceuticals Forum) + pharmaceuticals	40
9	(Central eastern European and Southern eastern European Countries Initiative) + pharmaceuticals	40
10	(Fair and Affordable Pricing Initiative) + pharmaceuticals	40
11	(Visegrad+2 Group) + pharmaceuticals	40
12	(Southern European Initiative) + pharmaceuticals	40
13	(WGEMA collaboration ³) + pharmaceuticals	40
In Russian		
1	прозрачность цен лекарства	100

2. Cross-country collaboration in the area of health technology assessment among Finland, Norway and Sweden.

3. Nordic Council Working Group on Exchange of Information and Experience in the Medicines Area.

Other websites

Other websites in English were:

- EU Alliance for Innovation and Access email listserv (2): “France, transparency”; “Italy, transparency” – top 50 hits screened; and
- Knowledge Ecology International (3): “transparency” – top 50 hits screened.

Another website in Russian was:

- Commonwealth of Independent States legal acts database (1): лекарства цены прозрачность; лекарства прозрачность – first 100 hits screened for each search term.⁴

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4. The first search term had 2085 hits and the second search term had 316 hits.



ANNEX 2. GLOSSARY

Distributor remuneration. A mark-up or margin that can contribute to the ex-factory, wholesale or pharmacy retail price, or a service fee rendered to distributors (e.g. wholesalers or pharmacies) (1).

Ex-factory price (synonym: list price). The price charged by a pharmaceutical manufacturer, also called the manufacturer's price. This price can be lowered by agreement, resulting in the net price (1).

External reference pricing. The practice of using the price(s) of a pharmaceutical product in one or several countries in order to derive a benchmark or reference price for the purposes of setting or negotiating the price of the product in a given country (1).

Internal reference pricing. Price that is set in a reference price system, where the third-party payer funds a maximum amount (reference price), while the patient must pay the difference between the reference price and the actual pharmacy retail price of the medicine, in addition to any further co-payments (e.g. prescription fees, or percentage co-payment rates) (1).

Managed entry agreement (MEA). The formal arrangement between payers and manufacturers with the aim of sharing the financial risk due to uncertainty surrounding the introduction of new technologies that have been developed and introduced in order to enable access to new medicines (2).

Net price. The amount actually received by the supply chain actors (i.e. manufacturer, wholesale, pharmacy retail), after subtracting rebates, discounts and any other incentives (3).

Pharmacy purchasing price (synonym: wholesale price). The ex-factory price and the wholesale mark-up and the pharmacy mark-up (if the official distribution remuneration schemes specify the wholesale or pharmacy mark-ups) (1).

Pharmacy retail price. The price paid by patients when purchasing a medicine in a pharmacy. It is based on the pharmacy purchasing price but would contain any distributor fees added by the pharmacy. It might also include value-added tax (1).

Procurement prices. The price stated as the outcome of a procurement or tendering procedure. The tenderer that offered the most advantageous bid (with price as one key award criterion) is awarded (1).

Reimbursement price. The maximum amount paid for by a third-party payer (e.g. a health system or insurer) (1). If internal reference pricing is being used, reimbursement prices may be matched to reference prices.

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ANNEX 3. EXAMPLES OF NATIONAL LEGISLATION SUPPORTING THE TRANSPARENCY OF R&D COSTS OF MEDICINES, VACCINES AND MEDICAL PRODUCTS

In 2019 the Italian Minister of Health and Ministry of Economy and Finance signed a decree outlining new rules for negotiating pharmaceutical prices (1). The decree entered into effect in July 2020. Excerpts of the legal text are as follows (with only some parts of each article shown).

Art. 2 (Procedure for the submission of the negotiation application)

1. To access the procedure for the negotiation of the reimbursement and prices of the medicine, the company must submit to AIFA⁵ the application accompanied by the documents in compliance with the indications to be set out by deliberation of the Director General of AIFA, which shall be adopted no later than 30 days from the adoption of this decree.
2. The company must support its application with:
 - a) the scientific documentation showing any added therapeutic value of the medicine, in relation with the main treatments to which the medicine is compared. Such comparison shall take into account the therapeutic alternatives used in national clinical practice, providing evaluation and information elements that indicate the main treatments to which the medicine can be compared. In order to allow a comparative evaluation of the costs of alternative treatments, the posology schemes and the duration of the treatments must be explained;
 - c) self-certified information elements, with regard to the medicine which is subject to the negotiation, concerning marketing, consumption and reimbursement in other Countries and, in this case, at what price and reimbursement terms, including any further negotiation agreement;

5. Agenzia Italiana del Farmaco (Italian Medicines Agency).

- f) the forecast and changes in expenditure for the National Health Service deriving from the prices proposed, in the distinct components;
- g) the self-certified quantification of any public contribution and incentive aimed at research and development programmes regarding the medicine;
- j) any other information that may be useful for the purposes of the negotiation, including the patent status of the medicinal product.

Art. 3 (Negotiation procedure)

1. The negotiation procedure is finalized through the agreement between AIFA and the pharmaceutical company with the setting of reimbursement and price conditions, in accordance with the provisions of this decree, as well as taking into account of the following conditions:

- a) sales volumes;
- b) availability of the product for the National Health Service;
- c) discounts for supplies to national health service entities;
- d) contributions of a public nature to drug development and research programs.

2. When defining the agreement, it is envisaged:

a) the obligation to communicate annually to AIFA the sales, turnover, marketing costs and patent status of the medicine in Italy, as well as to report any discrepancies with respect to what was previously defined.

7. If there are no reference comparator medicines, the company shall submit economic evaluations according to the indications referred to in Paragraph 1 of this deliberation (determinazione) accompanied by adequate documentation aimed at explaining a price proposal, also based on the costs incurred for research, development, and production.

On 25 November 2019 the French Parliament adopted an amendment to the 2021 Social Security Financing Bill (2). An excerpt of the legal text is as follows.



Art. L 162-17-4-3

Companies make available to the Economic Committee for Health Products the amount of public investment in research and development from which they have benefited for the development of medicinal products registered or intended to be registered on one of the lists mentioned in the first paragraph of Article L. 5123-2 of the Public Health Code. This amount is made public. The conditions of application of this article are set by decree.

References

1. Decreto 2 agosto 2019. Criteri e modalita' con cui l'Agenzia italiana del farmaco determina, mediante negoziazione, i prezzi dei farmaci rimborsati dal Servizio sanitario nazionale (20A03810) [Decree 2 August 2019. Criteria and modalities with which the Italian Medicines Agency determines, through negotiation, the prices of medicines reimbursed by the National Health Service. (20A03810)]. Rome: Ministry of Health; 2019 (in Italian; <https://www.gazzettaufficiale.it/eli/gu/2020/07/24/185/sg/pdf>, accessed 21 February 2021).
2. Loi no. 2020-1576 du 14 décembre 2020. Loi de financement de la sécurité sociale pour 2021. Paris: Président de la République; 2021 (<https://www.legifrance.gouv.fr/loda/id/JORFTEXT000042665307/2021-01-29/>, accessed 21 February 2021).

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