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The enlightened decision

New pricing models for generic medicines to ensure long-term healthy competitiveness in Europe

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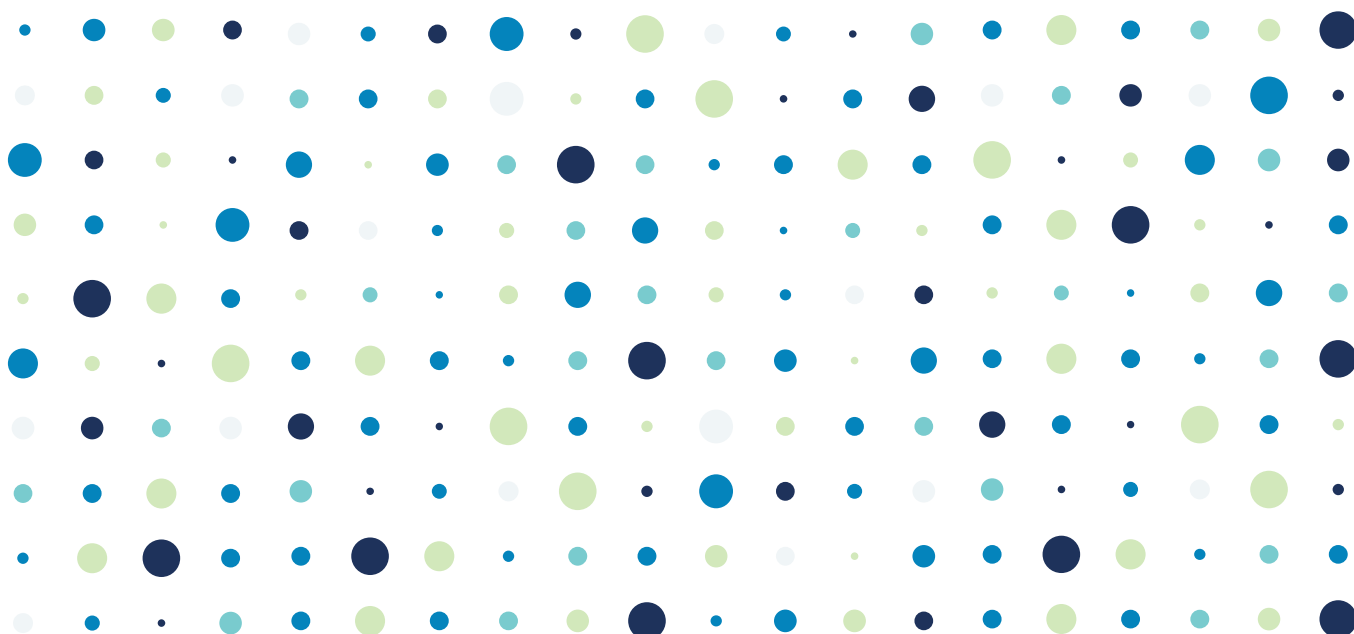


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1. Executive Summary

Generic medicines play an important role in the European healthcare system and economy. Not only, do generics impact the market (contribution to market supply), budget (substantial cost savings), and macroeconomic sector (employment, investments) but also, they positively influence patients by improving their health outcomes and medication adherence.

Most European countries regulate generic medicines prices using policy tools like external and internal reference pricing mainly to reduce medicines expenditures and generate savings which could be used to expand access to both innovative and generic medicines. External Reference Pricing (ERP) is not perceived as a proper tool to ensure competitive pricing in the off-patent market since off-patent medicines already operate in a highly competitive market environment and other policies are more appropriate to stimulate competition in the off-patent market. Internal Reference Pricing is the classical tool most widely used to harmonise prices of products with the same or similar therapeutic effect (the reference group), working best in association with other tools supporting the use of generic medicines. Without complementary measures to increase generic uptake, internal reference pricing provides no incentive to compete on prices at levels below the regulated price caps and free pricing would appear to work better.

The major issue mentioned by experts is the lack of a dynamic approach to create a link between the reference price and the level of competition within a certain reference group: if there are few competitors, the reference price can be increased, if there are many but without competition on prices – reduced.

With a more holistic approach, pricing policies can be used throughout all the product to revenue chain (the life cycle of the generic medicine – starting from launching it to the market until it generates revenue) for generic medicines in the retail market: they may impact the price, reimbursement, control of excessive spending and taxes/subsidies affecting the revenue. The efficient generic medicines policies facilitate patients' access to high-quality treatments through affordable medicines and provide substantial healthcare savings at the same time. Pricing policies have a significant influence on the shape of the generic market and may decrease competition level, causing market concentration, and jeopardising access to certain medicines, thus increasing health disparities if applied in an unbalanced overly restrictive way. Forced price reductions, clawback and other administrative budget control measures applied to the off-patent market may result in a low level of prices/revenues that impact economic viability and lead to voluntary withdrawals from the market further decreasing competition and deepening medicines shortages, which generates higher prices in the long-term. Several studies concluded that an increasing number of competitors contribute to healthy competitiveness enabling continued lowering of the prices.

At this point, there is no evident (clear-cut) universal approach that would balance the unsustainable generic market in Europe although decision makers should explore the availability of policies towards improving the competitiveness of generic medicines in their countries. A fundamental mindset shift is required to implement competition-sensitive approaches in policy models applied to generic medicines. The new pricing policy models described in this report are adequate to address this requirement. With the support of experts, three of the most promising new pricing policy models have been identified that can

improve the competitiveness in the off-patent market, these are: tiered pricing, de-linkage from the originator's price and an automatic indexation. A tiered pricing model responds to changing reference price system rules to allow MAH to decrease the price with new market entrants or increase the price in case competition is limited and supply could be at risk. De-linkage from the originator price model prevents the originator from forcing generic competitors' prices to economically nonviable levels. Automatic indexation models aim to compensate for higher costs due to inflation or rising regulatory burden by automatically adjusting prices based on a given index value. New pricing policies involving an additional end-user (patient) fee (hypothecated tax, cost allocation) are uniformly considered as having a very low implementation potential due to very low social acceptability. The rest of the assessed models/approaches - one-in-on-out (OIOO), tax credits, value-based pricing, volume for savings, price heaven and guaranteed margins/fees represent mid to low implementation potential according to experts and Medicines For Europe (MFE) members.

The most fundamental recommendation for decision and policymakers would be to start consistently monitoring the level of competitiveness in reference groups (using the Herfindahl-Hirschman Index), notice the changes in a negative direction and take action when deterioration of competition is considered a threat to continued supply, instead of waiting inactively until medicines are no longer supplied. To implement such competition-sensitive pricing policies, one must rely on sales and shortages data and their repeated analysis. To address the current challenges that we are experiencing in Europe, new solutions are needed. A robust dialogue between regulators and supply chain partners must be established to find the solutions that will best deliver a sustainable supply of medicines to patients.

2. Introduction

Generic medicines play a critical role in expanding access to affordable, high-quality therapeutic options for patients in Europe. The generic market concentration in Europe, caused by the generic manufacturer's withdrawal entails tangible medicines shortages. Among multiple factors contributing to generic manufacturers leaving the market, it is essential to recognise how European countries' pricing policies facilitate this negative trend by failing at promoting healthy competitiveness.

This report consists of two parts. The aim of the first diagnostic part of the report is to present current knowledge and experience of the impact of direct and intense price regulation of generic medicines on dynamic price competition among generic competitors in Europe. Additionally, the impact of the implementation of systems regulating the reimbursement rate, particularly through reference pricing and similar tools, is reported.

The second part of the report is aimed at new pricing models, their value and applicability for generic medicines in Europe. The feasibility and applicability of these new models across Europe are presented using the country archetypes. These are groups of countries which share similarities in approach toward generic medicines price regulation.

The study is based on Systematic and Targeted Literature Reviews and interviews and ad-board with experts from five countries (Belgium, Portugal, Spain, Romania and Greece) representing four-country archetypes.

The scope of the report includes the whole pricing framework that affects generic manufacturers: starting from setting the price of generic medicines through reimbursement level and patient co-payment up to rebates and payback, i.e., the whole product-to-revenue chain. The report focuses on the retail Rx market.

The market for prescription-only medicines consists of both innovative (protected or no longer protected by a patent) and generic medicines. It is generally recommended that the pharmaceutical market should be regulated with a broad picture in mind, so the balance is sustained (or restored) for all kinds of medicines on the market. Regulations regarding generic medicines should not be introduced without innovative medicines market analysis and consideration of the overall healthcare system organisation and objectives in a given country. Countries with more flexibility in terms of healthcare budgeting, such as Germany or the Netherlands, have relatively more options to allocate financial means and stimulate the generic sector as needed than countries with tight and highly regulated budgets.

- *“To enhance and promote the competitiveness of generic medicines...it shouldn't be separated completely from what happens for innovative medicine. So, I think that we should work on both*

*sides. On one side is the pricing of generics and competition and on the other help for innovative drugs to enter the market”. **

- *“Before talking about pricing per se, we have to take into account and into consideration some overall principles and to relate it to the healthcare objectives and to what extent these principles really are fulfilled or are accomplished within the model that you present us”*
- *“Anything that helps driving that flexibility in prices – with a holistic view on the demand side for generics like the UK for instance, I would support”.*

Such a holistic approach to generic pricing should be adopted considering different aspects of healthcare systems and needs of various stakeholders. Not only do generic manufacturers need to make profits to stay on the market and supply, but also fair pricing is necessary for patients so they can have access to affordable medicines. Pricing policies that allow for a long-term sustainability of the generic business model are the key enabler in term of access to high quality, affordable medicines. None of the proposed new pricing models for generics (even if proved to be feasible) can be successfully implemented if not endorsed by decision-makers or if it stands in opposition to public interest or expectations. Various stakeholders that have a key interest in availability of affordable medicines, should be properly represented in the decision-making process, to come up with efficient and sustainable strategies.

In search for new pricing models that might be applicable to the generic market it is essential to not exclusively focus on the competition aspect, but also on the sustainability of the market. Both aspects are equally important to be carefully evaluated, especially in terms of implications.

- *“Some countries try to establish a level playing field where they wish to align the price of the originator with the generic medicines and other countries want to create a price differential between the generic and the originator. And I think you need to explore very carefully what the implications of that are for competition and the level of sustainability of the market.”*

The report notices the fact that the European medicines market, including the generic market is facing the unprecedented cost pressure caused by post-Covid-19 “reality”, inflation and the war in Ukraine.¹ These events have imposed the need for future-proofing pharmaceutical legislation that would compensate for the multidimensional burden placed on the medicinal sector.²

The second part of the report is providing an overview of potential solutions: new policy models that could be applied to generic medicines and ensure healthy competitiveness and economic viability.

Europe’s generic medicines supply is severely impacted by the complex economic situation caused by the recovery from the Covid-19 pandemic, soaring inflation and recently also by the war in Ukraine. Medicines, especially generic medicines, are essential nowadays not only to fulfil European citizens’ health needs but

*Formatting in italic with bullet points is reserved in the report for quotations from interviews with invited experts or from the advisory board meeting with them.

also to help save and improve the health of war refugees. However, the generic medicines sector might not have the capability to provide for all due to unprecedented cost pressure. Prices of energy, fuels, and ingredients (raw materials) have increased significantly. Logistics and transportation also started producing extra costs as the global supply chain has been forced to adopt new shipment channels to avoid ground transfer via the Ukrainian territory. There also have been some complications regarding the supply chain network relying heavily on the consolidated Asian market that was unstrung during the Covid-19 pandemic.

Raw materials prices skyrocketed mostly due to inflation. In the most extreme cases, the price has grown by 180 percent compared to last year.

Taking into consideration all additional costs that generic manufacturers must cover, being at the same time under pressure by European pricing policies, it does not come as a surprise that many of them might become economically unviable. There is a tremendous need for support coming directly from Europe to prevent generic medicines shortages and supply disruptions.¹ Both legislative and non-legislative solutions should be on the table along with a comprehensive medicines shortages monitoring system focusing on medicines with a high risk of supply issues – off-patent and generic medications.

It is vital for new legislative frameworks to manifest a future-proofing characteristic understood as resilience toward unknown events on a global scale such as wars or pandemics. There should be a response to exceptional financial burdens placed on healthcare systems and generic companies impacted by the war in Ukraine, inflation and the post-pandemic, unstable global situation. There is no sustainable future growth and development without systemic changes (new pricing policies, promotion of healthy competitiveness and market concentration preventive measures) regarding sectors that are critical for Europe. The deterioration of the current situation on the generic market is anticipated if any effective measures would not be undertaken to buffer the long-term negative impact of economic crisis and disrupted global supply chain caused by the military conflicts.²

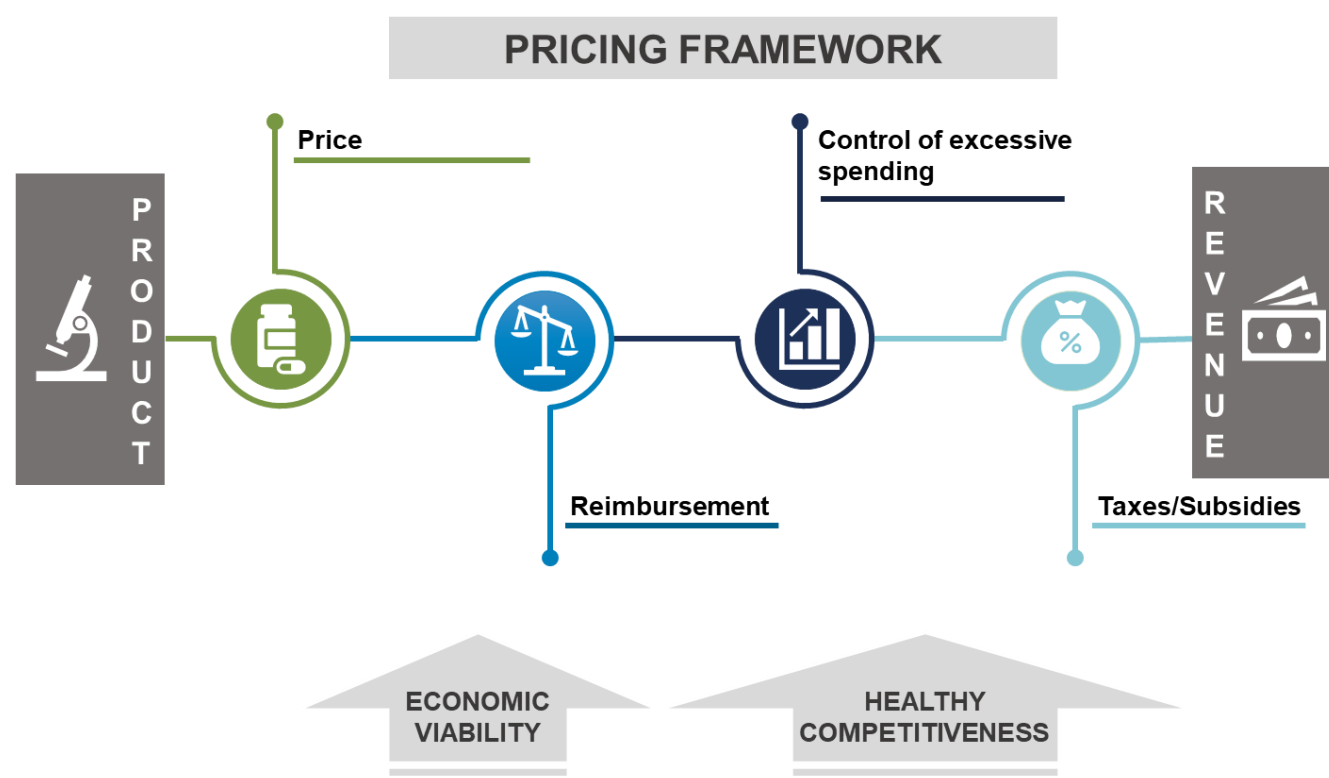
3. Product-to-revenue chain of regulations and policies – from the manufacturer's price through the patient co-payment level up to rebates and payback

The aim of this chapter is to present the pricing policies that are currently used in European countries to regulate the generic medicines market. At the beginning, the definition of the pricing policy on generic medicines for the purpose of the report is presented. Then, an overview of the current pricing policies on generics in European countries with some historical changes where available is given. Finally, countries' history, as available, including publicly stated goals and objectives identified to be addressed by a given policy in each country when it was implemented or modified is reported.

3.1. Product to revenue chain – the Pricing Framework

For the purpose of the report, pricing policy will be understood as all pricing regulations that affect generic manufacturers, starting from setting the price of their products through reimbursement level and patient co-payment up to rebates and payback which affect the total revenue of generic medicine manufacturers (product to revenue chain, Scheme 1). Only the retail prescription medicines market is considered.

Scheme 1. Product to revenue chain – the Pricing Framework



In the debate on current and new pricing models for generics, it is essential to distinguish between pricing and reimbursement. These two terms are often used interchangeably incorrectly and may mislead the recipient.

Price is a collective term which can cover both ex-factory price and wholesale or retail price while reimbursement may refer to the amount of reimbursement (sometimes called reference price or reimbursement limit) or reimbursement level (percentage of the price that is publicly funded). Some policy tools only impact on price, others, although also known as pricing policy tools, only impact on reimbursement, while some impact both on price and reimbursement.

Therefore, it is fundamental in the debate on new pricing tools for generics to define specifically which place of the product in the revenue chain framework we are talking about.

3.2. Current pricing policies on generics in European countries

Almost all of the analysed countries use price regulation while free pricing is implemented in the UK and Denmark. Germany and the Netherlands have a mixed system – partially free pricing but with tendering, discounts by law, preference policy, and internal or external reference pricing.³

The majority of European countries adopted a reference pricing system to control and regulate the generic market. The foundation of reference pricing is to establish a reimbursement level or reference price for a group of interchangeable medicines.¹⁹ Reimbursable medicines are typically subject to a price control whereas non-reimbursable medicines are allowed free pricing. The same applies to reimbursable and non-reimbursable generics.¹⁴ Theoretically, medicines manufacturers, including generic manufacturers, have the freedom to set prices, although establishing a medicine's price above the reference level entails an additional patient co-payment. It may even lead to not being included in reimbursement if the price exceeds the acceptable reference level, as it is a common practice in Europe that medicines need to be priced below the reference level to be reimbursed.¹⁹

At the manufacturers' level, most countries set control only over reimbursable medicines that are partially covered by national health services or health insurance companies. Few European countries attempt a price regulation for all medicines, regardless of their reimbursable status. On the other hand, the lack of a price control over reimbursable off-patent medicines is characteristic of free pricing countries represented by Denmark, Germany, and the UK. Whereas Germany and Denmark are considered free pricing countries, they have some long-operated price control tools that can be applied to generics.¹⁴

The overview of the current pricing policies on generics in European countries with some historical changes where available is presented in Table 1. Data about current pricing policies in European countries are taken from Market Review – European Generic Medicine Markets, MFE 2020.³

In the Appendix, tables with detailed characteristics of classic pricing tools are provided.

3.2.1. External reference pricing

External (international) reference pricing (ERP) is the practice of comparing the price of pharmaceutical products in different countries to set a benchmark price.⁴ Mostly, price controls apply to reimbursable medicines, whereas non-reimbursable medicines are usually priced freely. Also, prices are set by the pricing authorities alone or are negotiated between the manufacturers and the pricing authority.⁵

The purpose of external reference pricing is to assess the adequacy of pharmaceutical pricing, based on selected benchmark countries, in order to establish or negotiate a product's price in a given country. Depending on the design of the policy, external reference prices seek to ensure that the country does not pay more than other comparable countries.⁴

The selection of suitable and comparable national benchmarks is one of the main steps in the implementation of external reference prices. Selection criteria include location, country income, medicine availability, country of origin and market size. The basket of the reference countries is calculated individually for each country. Some countries have specific restrictions regarding the number of countries in the basket. Additionally, some of the European countries require having in the basket at least 50% of the countries with an already established price of reference product – this requirement simplifies the process. The size of the basket of reference countries varies, from 3-4 countries for France, Portugal, Croatia and Cyprus to even more than 20 for Austria, Italy and Poland.⁶

Prices are compared at common points along the distribution chain from manufacturer to wholesaler to retailer.

The methods for calculating the conversion of reference prices to final price vary among countries using external reference prices. Countries may choose the lowest price, the average price, or the average of the lowest prices. Others also adjust prices for factors such as market size and currency strength.⁴ Price re-evaluation (after the initial price is set) can be carried out annually, twice a year or more or less frequently.⁶

According to the Euripid Guidance Document, ERP is not a suitable price control mechanism for ensuring an appropriate and competitive price environment for generic and biosimilar medicines. Off-patent medicines already operate in a highly competitive market environment and other policies are more appropriate to stimulate competition in the off-patent market.⁷ ERP is not a tool that regulates prices effectively and has multiple unintended consequences that reduce its overall benefits and potentially positive impacts.⁸ All experts agreed that internal reference pricing has a much higher potential than ERP for setting generic medicines prices.

However, external reference pricing is a policy widely adopted in many European countries, both in high- and middle-income countries and other regions⁴. For the majority of countries, ERP is the main criterion for price setting, but for some (Poland, Italy, Spain) ERP is a supportive criterion for price-setting (informative role) and in Hungary, it is used only once at launch.^{6,8} External reference pricing (ERP) implementation varies greatly among European countries, as does the impact it has on national generic markets⁸. Other countries are also considering the implementation of external reference pricing.⁴ Among the analysed countries half of them use external reference pricing (Bulgaria, the Czech Republic, Greece, Ireland, Lithuania, the Netherlands, Poland, Portugal, Romania, Slovakia).

3.2.2. Internal reference pricing

Internal reference pricing (IRP) compares the prices of pharmaceutical products that are therapeutically similar and can be interchanged for one another, within a country.⁴

Therapeutic comparability and interchangeability are determined by the chemical entity and pharmacological class according to the Anatomical Therapeutic Chemical Classification (ATC) System 9 or by the therapeutic indication.⁴ IRP in the majority of European countries is based on ATC-5 which means the same active ingredients, but some countries also allow ATC-4 (chemical subgroup) or a mix of different ATC levels.^{3,9}

The purpose of internal reference pricing is to limit the price paid by governments/payers of products with the same or similar therapeutic effect in order to reduce price volatility among comparable products. Internal reference pricing works best if countries have policies supporting the appropriate use of generic and biosimilar medicines.⁴

The reference price can be established by considering factors such as active ingredient, dose, and method of administering the product and package size. Prices of these products would be compared and set according to the evidence of equivalence and at common points in the distribution chain.⁴

The methods for calculating reference prices vary among countries using internal reference prices. Countries may choose the lowest price within the group, the average price, the average of the lowest prices or a percentage below the original (generic price link).

Setting prices at the specified level of the original medicine is called price-capping. The level of mandatory reduction varies by country. The highest percentage below the originator price is in France and Ireland (60%) and the lowest in Romania (35%). Austria, Slovakia and Hungary have three levels of price-capping, for the first, second and third generic after the originator.³ Detailed values for all countries are presented in the Appendix. Price updates can be carried out every two weeks, monthly, quarterly, every 6 months or annually.⁹

IRP has several advantages. Firstly, IRP makes patients and physicians more price-sensitive, especially if patients are well informed about product alternatives. If a patient chooses a higher-priced medicine within the same reference group, he has to pay the difference between the actual and the reference price. IRP forces companies to enter into price competition, as they may choose to reduce prices in line with the reference price in order to keep or increase their sales.⁹

The World Health Organization (WHO) suggests the use of IRP for generic and biosimilar medicines using the principles of generic reference pricing, under the following conditions:

- IRP is used in conjunction with policies to promote the use of quality-assured generic or biosimilar medicines,
- reference prices are obtained and validated from verifiable data sources,
- consistent and transparent criteria for pricing of generic and biosimilar medicines are explicitly evaluated and stated based on an established methodology.⁴

Experts agreed that IRP has quite a lot of potential to enhance healthy competitiveness in the generics market. Germany was mentioned as an example of successful use of IRP for generics but also needs

some improvements, for example, to reduce the level of patient's co-payment for some classes of medicines.

- *“Germany’s example is very interesting. The groups are not formed only by the same agent, but also by therapeutic similarity”.*
- *“One important thing is not to base only the homogeneous group on the basis of the active ingredient, but be a little bit wider, so based on therapeutic similarity”.*
- *“We can make smarter use of internal reference pricing systems, and I refer to the example of Germany. They look at the level of competition per reference group and if they see in a specific reference group that there are fewer suppliers available then they raise the reference price. And that obviously provides an incentive for manufacturers to enter into the market. And maybe in another reference group, when they see that there are multiple suppliers on the market, then they reduce the reference price in order to promote price competition”.*

Experts also indicated that reference pricing should be more dynamic and dependent on the level of competitiveness. Indicators of competitiveness are described in 5.3.1.

- *“We should move to the more dynamic reference pricing system in order to promote healthy competitiveness. And it basically means that I would tie the reference price to the level of competition within a certain reference group. If there are few competitors, we can raise the reference price and if there are many competitors, we can promote competition by reducing the price.”*

All analysed countries with price regulation policies, implemented internal reference pricing. The only exception is Sweden.

3.2.3. Control of Excessive Spending (payback, clawback, rebates, and discounts)

Payback and clawback policies aim at preventing budget overspending, by claiming refunds from the industry once a target budget is exceeded.⁵ The scope for calculating a budget varies by country and can be a global or segmented pharmaceutical budget or defined by the pharmaceutical expenditure growth rate.³ Also bases for calculations of payback and clawback are different among European countries and it can be market share, revenue, or growth.

Payback policies require manufacturers to return some of their revenue if a predetermined budget ceiling for public pharmaceutical expenditure is exceeded. In some cases (e.g., Hungary) payback is automatic and mandatory independently of the status of pharmaceutical expenditure. In Greece payback is limitless, meaning that there is no maximum level of payback put on generics manufacturers.

Sometimes clawback is applied in place of a payback.³ Romania and the Netherlands have differentiated payback for generics. The payback period can be defined as two months, quarterly or annually.³

Clawback rules are usually applied to pharmacies. Clawbacks capture discounts on pharmacy dispensing fees or discounts on medicine purchases by pharmacies. The rationale for clawback mechanisms is to take over these discounts that increase the profit of pharmacies and pass them on as income/revenue to the public payer.³

Extraordinary contribution is in place in Portugal applies to net sales of medicines.

Rebates, discounts, extraordinary contributions, clawback and payback policies are widely used and powerful policy tools for cost-containment. Especially in countries where growth rates in pharmaceutical expenditures are high and more difficult to predict, or where price reductions are difficult to obtain, they are practical tools for generating savings.⁵

3.2.4. Retail tendering and negotiations

Tendering is any formal and competitive procurement process through which tenders (offers) are requested, received, and evaluated for the purchasing of products such as medicines or vaccines. The process is based on predetermined criteria, including price, product quality and value for money.⁴

Negotiations are discussions aimed at reaching an agreement with potential suppliers. The contract is awarded to the suppliers making the best offers. In addition to the acceptable general terms and conditions, the outcome of the tender and negotiation may include specific price reductions through discounts and rebates.⁴

The purpose of tendering is to encourage competition between potential suppliers. In some countries (e.g., Poland) negotiations are used to establish terms relating to various aspects of the procurement (e.g., price, quality, risk, payment schedule) between the negotiating parties or to facilitate the resolution of any remaining disputes regarding the terms of the offer. Tendering and negotiation may be done separately or together, or to supplement other pricing policies.⁴

Tendering and negotiations are recommended by WHO as one of the core methods of procurement but in the reality, it is quite rare and generally driven mainly by the price (lower-income countries). In higher-income countries, tendering has been used primarily in hospital settings and public services, such as pandemic plans and human papillomavirus vaccines.⁴

Within the context of this report, tendering is considered only if it concerns the retail (pharmacy) market.

Among analysed countries, negotiation of generic prices is not a common practice. Only Lithuania and Poland have implemented this instrument. Also, retail tendering is present in a minority of countries (Germany, Italy, the Netherlands, Slovakia and Spain).³

Table 1. Pricing policies in European countries³

Country	Pricing system	Reference pricing		Negotiation of generic prices	Control of Excessive Spending		Retail tendering
		External	Internal		Clawback/Payback	Generic specific budget-over-limit measures	
Austria	Price regulation	NO	YES	NO	NO	NA	NO
Belgium	Price regulation	NO	YES	NO	YES	NO	NO
Bulgaria	Price regulation	YES	YES	NO	YES	NO	NO
Czech Republic	Price regulation	YES	YES	NO	NO	NA	NO
Denmark	Free pricing	NA	NA	NA	NO	NA	NO
Finland	Price regulation	NO	YES	NO	NO	NO	NO
France	Price regulation	NO	YES	NO	YES	NO	NO
Germany	Free pricing & Price regulation	NO	YES	NO	YES	NO	YES
Greece	Price regulation	YES	YES	NO	YES	NO	NO
Hungary	Price regulation	NO	YES	NO	YES	NO	NO
Ireland	Price regulation	YES	YES	NO	NO	NA	NO
Italy	Price regulation	NO	YES	YES	YES	NO	NO
Lithuania	Price regulation	YES	YES	YES	YES	NO	NO
Netherlands	Price regulation	YES	YES	NO	YES	YES	YES
Poland	Price regulation	YES	YES	YES	YES	NO	NO
Portugal	Price regulation	YES	YES	NO	YES	NA	NO
Romania	Price regulation	YES	YES	NO	YES	YES	NO
Slovakia	Price regulation	YES	YES	NO	YES	NO	YES
Spain	Price regulation	NO	YES	NO	NO	NA	YES
Sweden	Price regulation	NO	NO	NO	NO	NA	NO
UK	Free pricing	NA	NA	NA	YES	NO	NO

NA – not applicable

3.3. Examples of implementation of classic pricing policies in European countries

Several examples of implementation of classic pricing policies are presented below together with their short- and long-term impact where available. One has to note that effectiveness and success for one stakeholder can be a major challenge for another.

Greece

In the decade 2000-2010, Greece struggled with two major problems in the area of the pharmaceutical market: public expenditure on outpatient pharmaceuticals was the highest in the EU and consumption of generics was very low by EU standards. Insufficient use of generics was partly due to generic prices being very high, fixed at 90% of the price of the branded product and a lack of price competition between them. Also, time to market entry was long.⁵

To control the overall level of expenditure, significant price cuts – especially for generics, and clawback were introduced in Greece in 2012 for all outpatient medicines, while in 2016 it was also applied to hospital medicines. The mechanism sets budgetary ceilings for expenditure, and any surplus should be returned to the State by the MAHs. At the same time, a mandatory logarithmic rebate has been established for all reimbursed medicines based on the brand, currently ranging from 14% to 30% of their factory value.^{3,10}

However, clawback escalated over time, from 78 mn € in 2012 to ~840 mn € in 2020 for the outpatient sector. Total rebates and clawbacks in 2019 were ~1.9 bn €, corresponding to over 40% of the medicines' ex-factory prices on average. The ever-increasing clawback burdens generics by affecting their net prices and by distorting competition.³

The generic medicines market share in Greece is one of the lowest in Europe and still below 40% despite a steady increase in the recent 5 years. The reason for this may also be the lack of incentives at the pharmacy level i.e., the margin structure which induce the use/dispense of the ever-expensive alternative (i.e., the originator) and the overall negative patient perception for generics.

The newest data indicate that mandatory rebates and payback in Greece are the highest across the EU, accounting in 2021 for ~42% on average over the ex-factory price of generics.¹⁰

Portugal

Reducing overall pharmaceutical expenditure and ensuring the cost-effective use of pharmaceuticals has been identified as a policy priority in Portugal. In the context of generics, it was crucial to increase their use.^{5,11} To control the overall level of expenditure during the last financial and economic crisis the Government created and introduced a new tax obligation (tax system) concerning the pharmaceutical industry (Extraordinary Contribution on Pharmaceutical Industry) that's purpose was to assure the sustainability of their NHS. This new tax obligation, approved for the first time within the Portuguese State budget for 2015, has been annually renewed and approved in every State Budget since then.

The contribution is based on human medicines, medical gases and derivatives of human blood and plasma sales. The payment is applied to net sales and is done on a quarterly basis. The low consumption was partly due to important legal and administrative hurdles that considerably delayed the effective entry of generics into the market. To increase the use of generics in Portugal, several policies over the past few years have been implemented, including mandatory INN prescriptions, pharmacy substitutions, homogeneous groups and reference prices which establish a maximum amount to be reimbursed, according to the reimbursement rate. The reference price corresponds to the average of the 5 lowest prices of the medicines that make up each homogeneous group. The maximum sales price of generics is set by reference to the price of the reference medicine. The price of the generic cannot exceed 50% of the maximum sales price of the reference medicine or 25% of that price, should the reference product's wholesale price be lower than €10. With a view to being reimbursed, the maximum sales price of generics entering the market, after a group of 4 generics, must be at least 5% lower than the price of the cheapest generic already approved (up to a limit of 20% of the reference medicine's maximum sale price). Such policies were expected to significantly increase the share of generics to 60% in terms of the outpatient market volume.¹¹ However, despite these measures, the market share of generic medicines has grown slowly in the recent 5 years to 57.6% of the Rx market in units.

From 2006 to 2020 generics suffered a price erosion above 67%.

The Netherlands

The Netherlands installed in 2007 a system of preference policy and tendering in the pharmaceutical market. This system gives health insurers high buying power on the market and drove prices down to a European minimum. But, at the same time, the Dutch government kept the external reference pricing and reimbursement system in place. Last year (April 2021) the reference pricing model was modified with Norway (not in the EU, not in the Euro zone) to become a reference country for pharmaceutical prices in the Netherlands.

In the Netherlands, there are high fines. For instance, in 2018 the Netherlands raised the maximum imposable fine on MAHs for culpable failure to meet supply obligations from € 150,000 to € 820,000. In a 2019 report, it was indicated that the effects of the enforcement of this measure were not yet known and could be either positive or negative.¹² At the same time, health insurers give high penalties if the demand is not met by the pharmaceutical industry. Because of the low margin and high risks for the industry, a lot of generic products left the market.

Generic products which have left the market, come back to the market as compounded products which are not controlled by price or reimbursement law.

Ireland

In Ireland, prices of generics were reduced by 20% in 2007, 15% in 2009 and another 40% in 2010. As a result, the prices of generics have been revised. In addition, wholesalers' margins and pharmacy margins were significantly reduced. Some of these measures have been successful in reducing expenditure on patented, off-patent and generic medicines. However, the impact on expenditure over a longer period of time is rather limited. Supplementing such pricing measures with policies that control quantity and

consumption may be necessary to promote the rational use of pharmaceuticals. This would make the pricing measures more effective.⁵

Ineffective attempts

All measures introduced in Spain between 1997 and 2006 to contain the growth in pharmaceutical expenditure were ineffective in the long term. These cost-containment measures included reviews of the reference pricing system, ex-factory price reductions, mark-up adjustments, prescription incentives and the exclusion of medicines from reimbursement. Possible reasons for the failure of these measures were that the price cuts were counterbalanced by more prescriptions, prescription doses increased, more expensive instead of cheaper pharmaceuticals were prescribed and new medicines for new treatments were added to the reimbursement list.⁵

Similarly in Belgium policy regulation on the promotion of generic medicines in the years 1995-2009 had no long-term effects.^{5,13} The regulations consisted of changes in reimbursement conditions, public tendering and entry of generic competitors to reference prices.

In every case, the main reason to introduce new policy measures was to contain costs or at least slow down the growth of pharmaceutical expenditure. With persisting budgetary constraints there comes determination which in some cases (e.g., Greece) may go much over the point of new balance and may introduce problems arising from being too effective (like medicines shortages).

Details of solutions in European countries are provided in the Appendix.

3.4. Key takeaways

- With a more holistic approach, pricing policies can be used throughout the products in the revenue chain for generic medicines in the retail market: they may impact the price, reimbursement, control of excessive spending and taxes/subsidies affecting the revenue.
- Most European countries regulate generic medicines prices using policy tools like external and internal reference pricing, clawback, payback or discounts, mainly to reduce medicines expenditures and generate savings which could be used to expand access to both innovative and generic medicines.
- Although widely used, External Reference Pricing is not perceived as a proper tool to ensure competitive pricing in the off-patent market, since off-patent medicines already operate in a highly competitive market environment and other policies are more appropriate to stimulate competition in the off-patent market
- Internal Reference Pricing is the classical tool most widely used (in all the analysed European countries except for Sweden) to harmonise prices of products with the same or similar therapeutic effect (the reference group), working best in association with other tools supporting appropriate use of generic medicines.
- As much as they are effective to generate savings, the mandatory rebates, discounts, extraordinary contributions, clawback and payback policies can easily be overused and severely impact

economic viability and sustainability of supply, especially if they are unlimited and lack differentiation to account for which products actually contributed to excessive spending with only 3 countries to differentiate payback for generics and innovative medicines.

- The major issue mentioned by experts is a lack of a dynamic approach to create a link between the reference price and the level of competition within a certain reference group: if there are few competitors, the reference price can be increased, if there are many – reduced.
- To maximise the saving opportunity and create the right balance, additional policies are needed on the demand side as well to incentivise off-patent usage (generic substitution or encouragement for patients).

4. Generic medicines marketplace in Europe: current state and dynamics

European countries share some major characteristics regarding the generic medicines market. However, a closer look at the pharmaceutical sector regulations, including generics, provides information about a variety of strategies existing to manage the generic market on a national level – there is no “one size fits all”. Each country needs to be analysed separately or at least within a frame of a country archetype to understand the context of the decision-making process and the main drivers of generic market dynamics. The understanding of existing national contexts is a cornerstone for further reflections about possible generic market reforms promoting fair competition.

4.1. Generic medicines – critical sector for Europe

In 2018, the European pharmaceutical industry generated around 765 thousand jobs and about four times more indirect workplaces. It is estimated that generic medicines accounted for 67% of all prescribed agents. Not only do generics help to reduce prices of medicines on European markets ensuring healthcare budget sustainability but also significantly expand patients’ access to affordable, up-to-date therapeutic options.

Within the territory of the EU, it falls under the competencies of the Member States to develop their own pharmaceutical pricing and reimbursement policies. There is no universal policy in place that would regulate specifically the generic market. A variety of regulations are allowed as long as they comply with the EU provisions, such as the Transparency Directive. Although there is EU harmonisation regarding marketing authorisation, countries can independently opt for more control over the pharmaceutical market, including generics and thus influence the competition within a sector.¹⁴ According to the current state, generic medicines are subjected to price control mechanisms in all European countries.

Experts emphasised the need to increase the role of the EU in regulating the generic drugs market. Harmonisation of regulations between countries and the development of universal guidelines for all member states is particularly important.

- *“We have to harmonise legislation as much as possible at the European or at the Central and Eastern European countries.”*

EU regulations prohibiting discrimination limit the possibilities of targeted assistance to a specific group of entrepreneurs without an equal opportunity of support for other market participants. On the other hand, within the European legislation, there are some exceptions for temporary use, which can be adapted to manufacturers of generics at risk of shortages. However, any introduction of such solutions must be done with the participation of the EU.

- *“I think there are opportunities within the European legislation to have some level of discrimination for a temporary time in order to avoid, for example, shortages because they are a public health*

crisis, but then you need to reflect on the legal provisions and the European legislation on how and to what extent you can accommodate for this.”

It is acknowledged in Europe, that efficient medicines policies are critical for increasing generics uptake.¹⁵ Consistent generic policy is the key to improve generics penetration (volume of generic market share) and enhance uptake. Better generics utilisation not only creates significant savings that can be allocated to innovations, but also helps to mitigate health disparities related to access to up-to-date medicines and standard of care.¹⁵ In the first decade of the XXI century, Italy, Belgium, Poland, and Spain were considered countries with a lack of a coherent generic medicines policy and underdeveloped generic medicines competition within the existing regulatory frameworks.¹⁶ Throughout the last decade however many European countries introduced amendments to their existing generic policies and thus have redefined the functioning conditions for generic medicines manufacturers.

Poland might be set as an example of a country in which since 2012 (introduction of a new law on reimbursement of medicines) the competition of generic manufacturers has been observed within the limit groups. Moreover, the Economic Commission in Poland is an institutional entity responsible for price negotiations of all reimbursed medicines, both on-patent and off-patent.

France on the other hand is a country with well-defined, long-standing generic medicines policies but certain regulatory measures have not been favourable to competition¹⁷.

Besides having an impact on competition, the generic policies along with a unique internal (national) healthcare system organisation can directly influence the generic medicines reimbursement. In the Netherlands, the preference policy introduced by healthcare insurance companies is the reason for drastic generic price reductions. Only selected generics are reimbursed and thereby the competition between generic medicines manufacturers who did not receive reimbursement is hampered. Government policy for all molecules, even if they are selected by the preference policy, must follow a reference price law and reimbursement law.¹⁸

While reflecting on the prescribing patterns of generic medicines in Europe, it is important to notice the polarisation between the role generics plays in European countries (there are some exceptions). There is a difference between countries in Western and Eastern Europe in the context of access to medicines. In Western Europe, generics' leading role is to generate savings and the secondary role is to expand access (because it is generally secured), while in Eastern Europe, the generics' primary task is to expand access to medicines with otherwise limited availability.

- *“We should consider the difference between Western Europe and Eastern Europe because in Western Europe, to be fair, all patients have access to the necessary medicines and generics are just being used to drive down prices, whereas in Eastern Europe not every patient has access to the originated product, and generic medicines play a different role. They do not only reduce price, but they increase access.”*

4.2. Reference pricing system and tools enhancing generic medicines utilisation

Generic substitution is possible to be endorsed in almost all European countries, excluding Austria and possibly Belgium, where generic substitution is limited to antibiotics medicines only. Some countries – Denmark and the Netherlands have already made generic substitution mandatory. In France, there is an incentive system in place to intensify substitution activities. Incentives contain the pay-for-performance remuneration scheme for physicians and higher profit margins for pharmacists. Typically, patients can refuse substitution, but this would require an additional out of pocket payment. In France, if the patient refuses substitution, it is expected that the full amount of the dispensed medicines would be covered out of pocket. Then, the patient can fill for partial reimbursement according to the 2019 French Healthcare budget law (Article 66)²⁰. Currently, it is estimated that about 80% of substitutable medicines in France are dispensed in their generic version, although national savings attributed to generic substitution are limited by the narrow scope of substitution (prescriptions within the Directory), which corresponds in value to 25% of the reimbursable medications. It is not expected for generics to surpass 20-25% of market share value in the foreseeable future under the existing – extremely narrow – scope of substitution. Supposedly, even if all medicines that could be, were dispensed as generics that would not produce significant growth of value. Despite some recent regulatory expansions, the French scope of substitution remains narrow and excludes from the Directory many off-patent medicines.²¹

Many European countries encourage prescribers to use the active substance name (INN) instead of the medicine brand name. INN prescribing, however, is not uniformly regulated across Europe.²⁰ INN prescribing is mandatory in Greece, Italy, the Netherlands, Lithuania, Portugal, and Spain. Optional INN prescribing is accommodated by the rest of the European countries, besides Austria, Denmark, and Sweden where prescribing by active substance is not legally allowed.³

Even though Germany is officially classified as a country with a free pricing model regarding generics,³ it utilised some indirect measures – the “*aut idem*” provision, to regulate generic prices to some extent. Pharmacists must dispense a medicine cheaper than the originator unless a prescriber ordered differently. In 2012, a similar regulation was introduced in Belgium. It is imposed on pharmacists to dispense a more affordable medicine, selected from among the three cheapest available options within the equivalency group if there is a non-proprietary name on the prescription.²⁰

4.3. Availability of generic products and European countries’ market penetration: volume and value dynamics

Technically, all European countries, including countries with a free pricing system regulate somehow their domestic generic markets in terms of price. A reference pricing system is often, in literature, referred to as non-competitive, meanwhile the free pricing model is believed to support a competitive pharmaceutical market environment, although both of those systems can drive down prices to an almost unsustainable level.¹⁹ However, if the volume of market share would be the measure of success, the countries with a free

pricing system – Germany, Denmark, and the UK³ are characterised by a higher level of generic medicines penetration¹⁹.

In Figure 1, Figure 2 and Figure 3 data about the Rx market in European countries are presented.²² Detailed methodology is described in Chapter 9.1. The Netherlands, Germany, and Poland are leaders in the European market with 81.1% and 78.7% and 76.5% respectively. At the other end of the spectrum are countries like Luxembourg (30%) and Greece (39.4%) with shares of 40% or lower. In most countries, there is an increase in the share of generics in the drug market. In several countries, such as Croatia, Hungary and Poland, this share remains at a similar level, and Lithuania and Romania have slightly decreased in recent years.

Figure 1. Rx market in European countries (1 of 3)²²

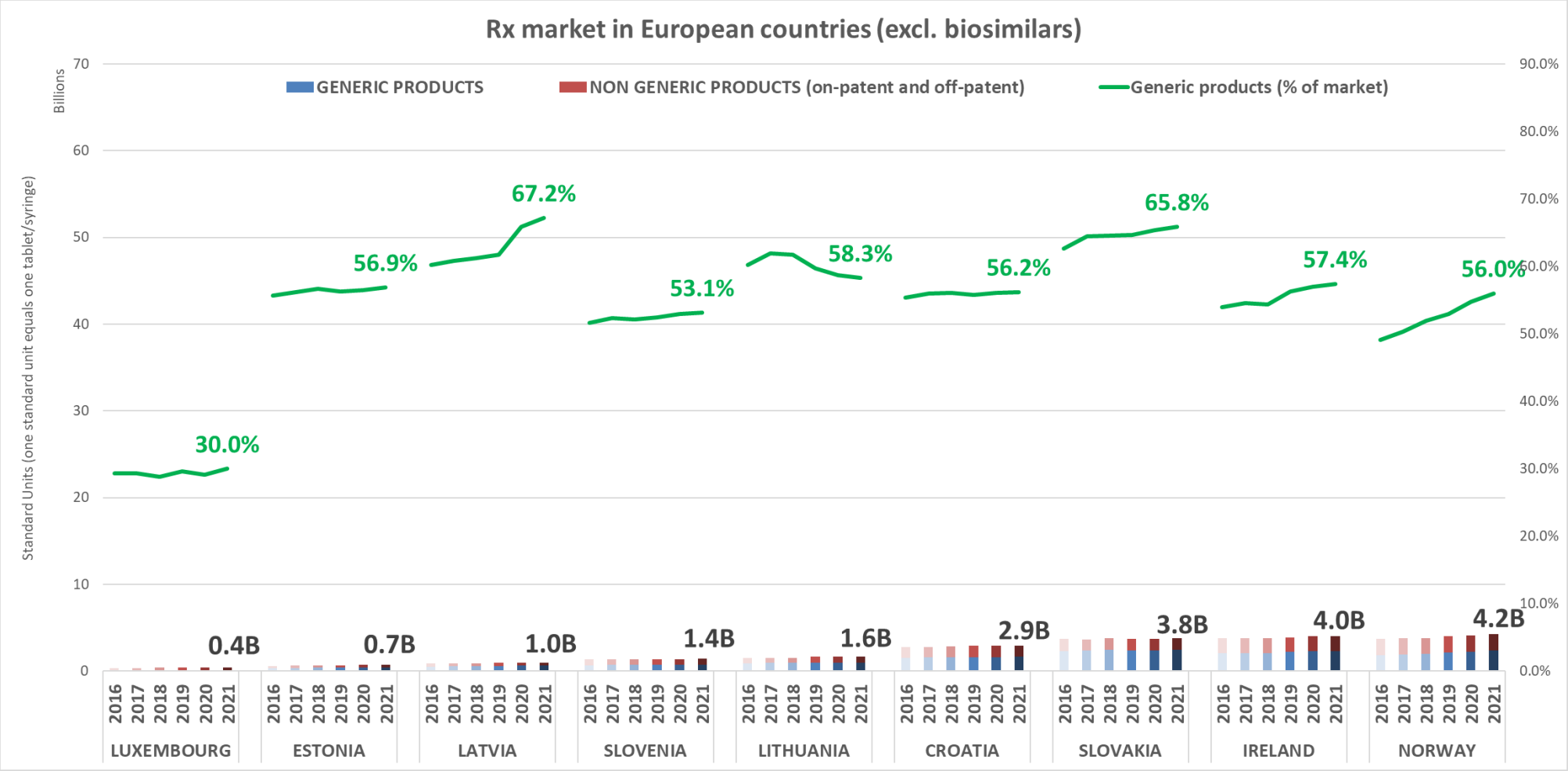


Figure 2. Rx market in European countries (2 of 3)²²

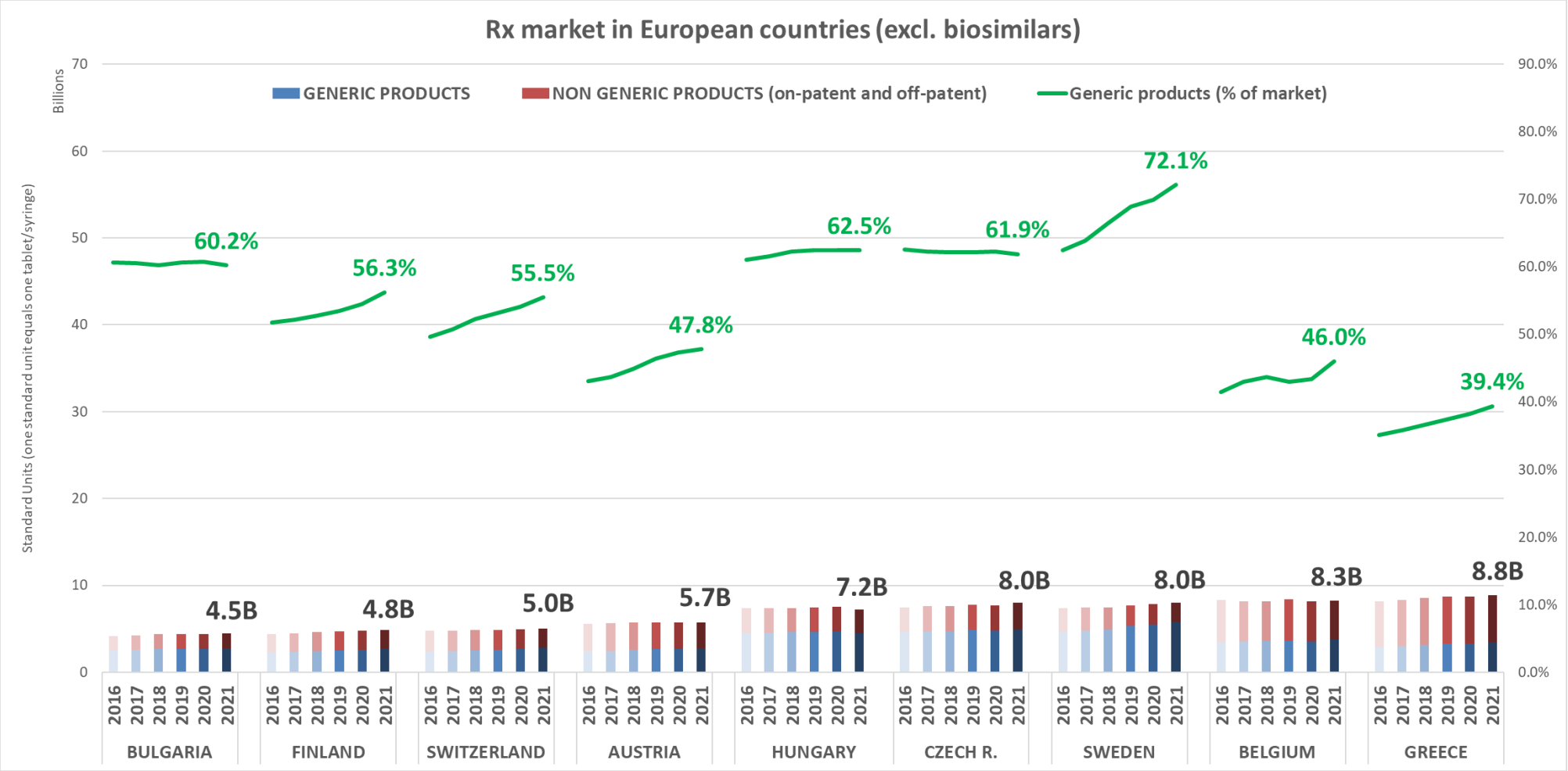
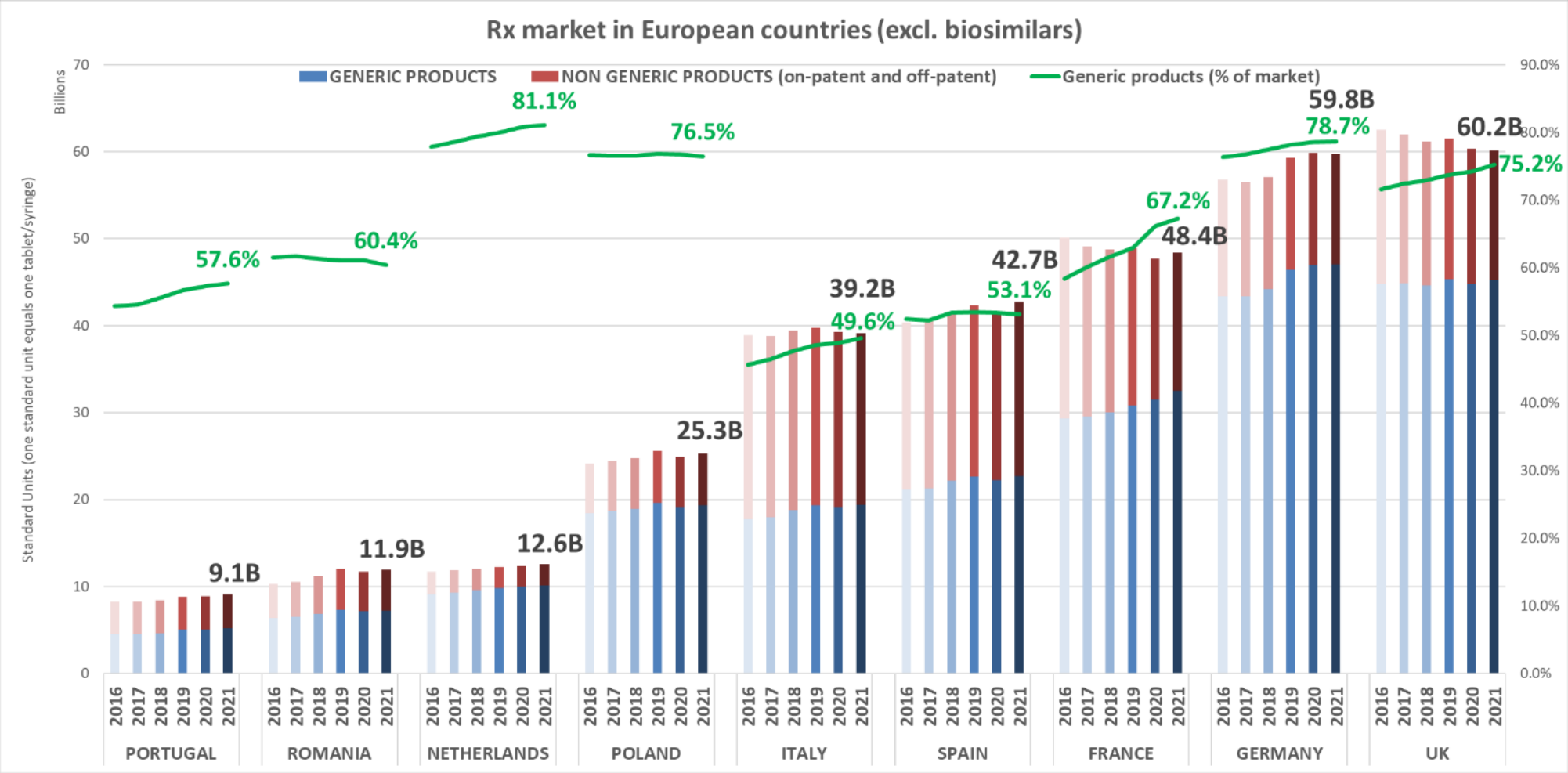


Figure 3. Rx market in European countries (3 of 3)²²



From a traditional perspective, generic medicines are considered in the context of their economic value and their contribution to medical supplies. It is not uncommon to observe European countries having a high volume of generic market share and noticeably low market value at the same time. This phenomenon is linked to generics' cost-reducing effect on the healthcare system (spendings). The average price of a generic, calculated for a specific European country that corresponds with market value, may not be a reliable measure of the generic market condition as it is impacted by various, country- and market-specific factors such as the higher price of medicines going off-patent. The high unit cost of medicines that recently have changed their status to off-patent has a consequence in generics seemingly increasing, relatively high prices.²³

Around 10 years ago, a significant drop (26.6%) in market value was observed in countries with a high generic market share, meanwhile, the same drop was insignificant (0.06%) in low market share countries. The market volume increased by approximately 29.3% in high market share countries and by 27.4% in low market share countries. The root causes associated with this rise were different though. In low generic market share countries, the volume increased due to intensified use of generic medicines while in markets with high generic market shares it was caused by improved utilisation and a shift from originator to a cheaper generic alternative. In terms of ex-factory prices, in high share markets, the price decreased by 43.2% and in low share markets, the decrease was less steep – 21.6%. No evidence was found that in the last decade this trend has changed in a significant way.²⁴

4.4. Generic medicines uptake

European countries' discrepancies in generic medicines uptake have their roots in multiple, different institutional settings and policies related to generic substitution. Generics uptake impacts directly both the volume of the market share and the ratio between volume and value. The price reduction is the primary indicator of cost savings induced by a generic market entry. It is estimated that prices can drop even by 70% on average within two years post generic market entry. In the light of a high diversification level between European generics policies and pharmaceutical market dynamics the saving potential related to generics has not been fully explored yet.²³

It is estimated that in July 2020 the generic volume sales in France reached 940 million boxes. This translates into one in three boxes of medicines sold in France being generic (38%). Objectively, it might be perceived as an impressive result, but the growth observed in 2020 in France, in comparison with the European average is insufficient. Higher use of generics could generate an additional €1.5 billion for the French healthcare system.²⁵

4.5. European countries experience with free pricing/ tendering markets

The main premise of the free pricing model is manufacturers' and suppliers' freedom in setting prices of their products, with the government relying on competition to keep prices low. Government intervention is expected only if competition does not seem to work. The highly competitive environment in the UK and

Dutch pharmaceutical markets has been driving generics ex-factory prices to extremely low levels. Prices have decreased so much that the UK experiences an economically unsustainable market for generic producers.²⁶ Even though, as stated above the UK and the Netherlands are European leaders in terms of generic market volume (85%). This percentage corresponds to only around one-third of the total market value (36%).²⁷ The average reimbursement price of generic medicine decreased from £5.01 to £4.03 between 2006 and 2017 in response to competition among multiple suppliers. During the same period, the average reimbursement price of brand medicines not only remained relatively stable but even experienced some increase from £19.71 to £20.73 due to not facing so intense manufacturers competition.²⁸ The UK's generic market competition may result even in a price reduction by 90% within the first couple of weeks after patent protection expiration.²⁹ Prior to the adoption of the free pricing model the UK carefully reviewed all available at that time (2001) pricing and reimbursement systems for generic medicines. The conducted analysis highlighted the advantage of a pricing system based on price-setting freedom over models based on direct price controls – tendering, reference pricing, profit controls. The UK's Department of Health have decided to implement free pricing in the name of significant savings for the taxpayers and supporting expanded patients access to medicines.²⁹

4.6. Generic medicines supplies and prices

The international difference in average generic prices also provides some perspective on generic companies' preferences while establishing terms and conditions regarding their product costs for selected European countries. The generic manufacturers do not set prices for their medicines equally in Europe, but instead, adapt them to the regulatory environment surrounding the pharmaceutical market in a certain country. Countries that are classified as mature generic markets (markets with an established, long tradition of generic utilisation) pay less for generic medications. Denmark, Germany, Poland,³⁰ the Netherlands, Sweden, and the UK are examples of mature generic markets. On the other side of the spectrum are developing generic medicine markets such as Spain,³¹ Portugal,³² France,³³ and Norway. Ultimately, the average generic price is the lowest in countries with a mature generic market that regulates prices.³⁴

4.7. Key takeaways

- The efficient generic medicines policies facilitate access to affordable, up-to-date medicines and provide substantial healthcare savings at the same time.
- With the current high level of diversity in country-specific policies, experts opt for more EU activity to harmonise regulations among countries, with a possibility to tackle medicine shortages at the EU level
- Consistent generic medicines policies are the key to improve uptake of generics and keep economic viability and healthy competitiveness.
- The Internal Reference Pricing system performs better if accompanied by other policy tools oriented towards increasing the uptake of generic medicines like generic substitution or prescribing

by international non-proprietary names. Moreover, the generics uptake can be improved if sufficient incentives for pharmacists and patients are in place.

- It is estimated that with increased uptake of generic medicines, considerable additional savings in some European countries could be generated.
- Countries with a long tradition of generic utilisation (mature generic markets) tend to pay less for generic medicines.
- While volume share reflects the level of market penetration by generic medicines, the value share is not a reliable measure to draw solid conclusions about the generic market situation in a certain country.

5. Impact of current pricing policies on generic medicines availability in Europe

The aim of this chapter is to assess the impact of current pricing policies on generic medicines availability in Europe. First, the sustainability of the generic medicines marketplace is defined. Then, consequences associated with generic medicines pricing policies are characterised. Among them, there is such as decreased competitiveness, which leads to market concentration, and in consequence medicines shortages and health disparities.

5.1. Sustainability of the generic medicines marketplace

The sustainability of health care budgets in Europe is under severe pressure from many factors, such as a growing and ageing population, increased burden of disease, introduction and rising costs of new innovative technologies and the impact of the COVID-19 pandemic and Ukraine war. To address these challenges, several national authorities have adopted austerity measures and applied short-term cost-containment measures to pharmaceuticals, including generics, despite their low cost (around 4% of total healthcare expenditure in Europe) and their importance for care (about 70% of the medicines currently dispensed in Europe are generic). Short-term cost reduction measures, such as ad hoc price cuts, external reference pricing, payback, tendering, etc. have resulted in the prices of some off-patent medicines dropping to an unsustainably low level. This is causing generic manufacturers to withdraw from the market, resulting in an increased risk of medicines shortages.³⁵

A sustainable generic medicines marketplace balances supply and uptake of medicines to ensure continued access.

5.2. Consequences associated with generic medicines pricing policies

Pricing policies aimed at increasing price competition among off-patent medicines by generic substitution, along with price referencing, are common in many countries. A key goal for public healthcare payers is to strengthen the allocative efficiency of healthcare costs. According to a WHO report on improving health system efficiency, *“allocative efficiency is allocating resources in such a way as to provide the optimal mix of goods and services to maximise the benefits to society.”*³⁶ In the healthcare context, *“allocative efficiency means that there is no alternative mix of health goods and services that could increase the health system’s final outcomes over the status quo.”*³⁶ The objective of a policy on generic medicines, considering that patients have full access to the originator or reference medicines before the expiry of a patent, is usually characterised by a reduction in health expenditure without compromising health benefits.³⁷ Despite this assumption in the reality there are some patient access limitation in several cases.

From an economic point of view, price regulation makes sense, unless there is a presumption that fair competition will generate a market price. This is the case for a producer that holds a monopoly, or if few

producers on the market compete and risk a duopoly, oligopoly, or price cartel. Price regulation is not necessary if there are more competitors in the market, and public authorities minimise the risk of a cartel. High mandatory price reductions for off-patent pharmaceuticals may cause a reduction in the incentive for producers to enter the market. This is especially true if deductions are combined with strict price regulations, for example, external reference pricing.³⁷

Achieving cost-containment through external reference pricing is limited due to several facts. Comparing pharmaceutical prices is difficult because published list prices may differ substantially from effective prices. This is due to different pricing regimes and little net price transparency. Profit margins for pharmacists and wholesalers and the value-added tax on pharmaceuticals differ across countries. Also, the industry negotiates discounts with distributors of pharmaceuticals, which are not communicated to the public and leave listed prices unaffected. Payback mechanisms may ex-post lower the effective prices of pharmaceuticals, but their impact on price levels is not published. Also, parallel trade may lower effective prices in high price countries. Packaging also differs across countries, making price comparisons partially invalid.⁵

The industry may adapt strategically and continuously to ERP, partially eroding the potential for cost-containment. Manufacturers can launch products in countries with high pharmaceutical prices first and thereby, prices may increase in all other countries which directly or indirectly refer to high-price countries. Moreover, the industry may avoid competition on prices and rather competes on discounts, which benefit wholesalers and pharmacies more than consumers. These adaptation strategies result in list-price inflation and cross-country convergence of prices. Consequently, ERP may lead to prices being relatively higher and not reflecting national market conditions. What is more, price reductions are not automatically translated into price decreases in referencing countries. This is because prices of pharmaceuticals are not reviewed instantly. Regular monitoring should therefore be ensured, possibly including all price changes, such as through discounts, which are not translated into changes in listed prices.⁵ On the other hand, too frequent price revision with ERP can generate extra price erosions like in Slovakia, where prices of generic and biosimilar medicines are set by external reference pricing at the average price of the three lowest prices in reference countries twice per year. This creates an unsustainable market as prices are very sensitive to market condition fluctuations in the reference countries (e.g., tender cycles). Some countries like Romania combine aggressive ERP at the lowest price of the twelve reference countries with a government clawback tax which results in a massive withdrawal of mostly generic medicines from the market.²²

ERP has been criticised for its potential to limit patient access to medicines. ERP becomes an incentive for pharmaceutical companies to adopt international pricing strategies. The “launch sequence strategy” is used to delay or avoid launching new medicines in countries with lower prices, especially if these are small markets referenced by countries with larger markets. There is evidence that pharmaceutical companies systematically delayed the past dossier submission in Belgium in order to avoid the Belgian price, usually in the low EU range, affecting other countries. It is also reported that the widespread use of ERP can determine circular pricing (the more countries are used as reference countries, the less clear it becomes

which country's prices are the reference). Price revisions in one country may, at least in theory, trigger a sequence of circular price revisions, further contributing to the strategic launching of new medicines.⁶

Internal reference pricing has also some disadvantages in terms of price regulation because it may lead to keeping higher ex-factory prices by producers anticipating that if they reduce prices, the health authorities will drive the reference prices further down. Also, within a reference price system, producers prefer to compete via discounts to pharmacies rather than through lowering list prices. Discounts are, however, to the detriment of the consumer, as pharmacies do not transfer these by lowering consumer prices.⁵

Besides ERP and IRP, there are other policy tools used by European countries that contribute to the unsustainability of the generic market.

In Spain, there is a reimbursement regulation stipulating no price difference between the originator and the generic medicines in most reference groups. This effectively eliminates any incentive for the uptake of generic medicines and will cause generic manufacturers to withdraw from the market further reducing competition and deteriorating patient access.

In France, at entry, generic medicines must be priced at least 60% below the originator's price, prior to patent expiration, and additionally, they undergo regular price cuts on a yearly basis.

In Portugal, the price of generic medicines has to be at least 50% below the price of the main market competitor (originator) and any change in the originator price entails a price reduction of the generic medicines. Such continued price linkage after generic medicines market entry stands in opposition to fair competition.²²

As shown by examples from different countries and in the literature, in a short period of time, reference prices meet their goal of reducing expenditure in the health care system. However, in the long run, the effect is quite the opposite.³⁸

The available evidence indicates that price-cap regulation leads to generic medicines prices' decreasing more than would occur without this regulation. In several countries with a reference price system, it has been observed that generics with a consumer price below the reference price do not apply price reductions until the reference price is reduced, even if there are other cheaper generics on the market (no price competition below the reference price). In addition to the price reduction imposed by the mere regulation of a price cap or reference prices, the entry of new generic competitors is useful to lower the actual transaction price of pharmacy purchases (dynamic ex-factory price competition), although the effect is weaker or insignificant for official ex-factory prices and consumer prices in some countries. When maximum reimbursement systems are used, such as reference prices or similar types, pharmacies receive large discounts on the price they pay for medicines, although these discounts are not passed on to the consumer price. The percentage discount offered to pharmacies in a country where a system of price caps is applied in conjunction with reference prices is positively and significantly related to the number of generic competitors on the pharmaceutical market (dynamic ex-factory price competition).³⁹ In Germany, medicines are assigned to "reference price groups" and a reference price is established for all products

within the same reference group to determine the maximum reimbursement price. That price can be decreased further than what was agreed. Since 2011 Germany has introduced price caps on medicines, including inexpensive generics, which forbid increasing reference prices even in line with inflation.²²

In some countries (not all – e.g., in Poland it is not allowed to offer a discount for pharmacies in the case of reimbursed products) with reimbursement systems using reference pricing or a similar mechanism, pharmacies appear to receive large discounts on the price they pay for medicines, although these discounts are not passed through to the consumer price. An example of such a situation is the Spanish generic medicines market. Price competition among generic manufacturers under the Spanish reference price system takes the form of large discounts on their NHS reimbursed purchasing costs, keeping the price paid by pharmacies low. These big discounts persist even after being legally banned, with an average discount rate of 39.3% on a purchase versus a pharmacy refund. This situation indicates that the consumer price of generic medicines is rigid, which prevents it from approaching the marginal cost of production, while at the same time the revenues generated by competition are shifted to the benefit of increased pharmacy margins.^{39,40}

For the purposes of this report, the systematic literature review (SLR) conducted by Puig-Junoy et al. was updated. Detailed methodology is described in chapter 9. Finally, 3 new publications were included in the analysis.

The aim of the study conducted by Tesar et al. was to investigate the impact of selected legislative initiatives and their implementation for off-patent medicinal products in Slovakia compared with the rest of the Visegrad Group (V4 countries).³⁷

The authors analysed the development of applications for the reimbursement of generic medicines. Particular emphasis was placed on the availability and penetration of generics from 2006 to 2020 in Slovakia and compared countries (the Czech Republic, Hungary, Poland, and Slovakia).³⁷

Detailed results of the study are presented further in this chapter in the context of examples from countries of the impact of pricing policies on the generic medicines market. The authors concluded that to increase utilisation of generic medicines, the comprehensive re-evaluation of combinations of the three-threshold entry, the number of mandatory price reductions, and external reference pricing requirements are required.³⁷

Granlund et al. conducted a six-and-a-half-year study in Sweden about the short and long-term price effects of the number of competing companies. Study results show, that in the long term the price of generics is found to decrease by 81% when the number of firms selling generics with the same strength, form and similar package size is increased from 1 to 10.⁴¹

The results also show that the effect of additional competitors is large also when the number of firms is already quite large. For example, going from seven to ten firms reduces generic prices in the long term by 21% when no functional form is imposed for the effect of the number of firms on prices. The authors tried to estimate how fast firms adjust prices to a changing number of competitors. For generic prices, 70% of the adjustment takes place within three months.⁴¹

Conclusions of this publication indicate that the large effect of the number of generic firms, also when the number is already quite large, implies that the pharmaceutical costs can be reduced substantially if this number was increased.⁴¹

The aim of a later study conducted by Puig-Junoy et al. was to test the hypothesis that under prevailing reference pricing systems for generic medicines, those medicines sold at a higher consumer price may enjoy a competitive advantage. Real transaction prices for 179 generic medicines acquired by pharmacies in Spain have been used to calculate the discount rate on acquisition versus reimbursed costs to pharmacies.⁴⁰

The authors concluded that under reference pricing there is intense price competition among generic firms in the form of unusually high discounts to pharmacies on official ex-factory prices reimbursed to pharmacies. However, this effect is highly distorting because it favours those medicines with a higher relative price in relation to the brand price before generic entry.⁴⁰

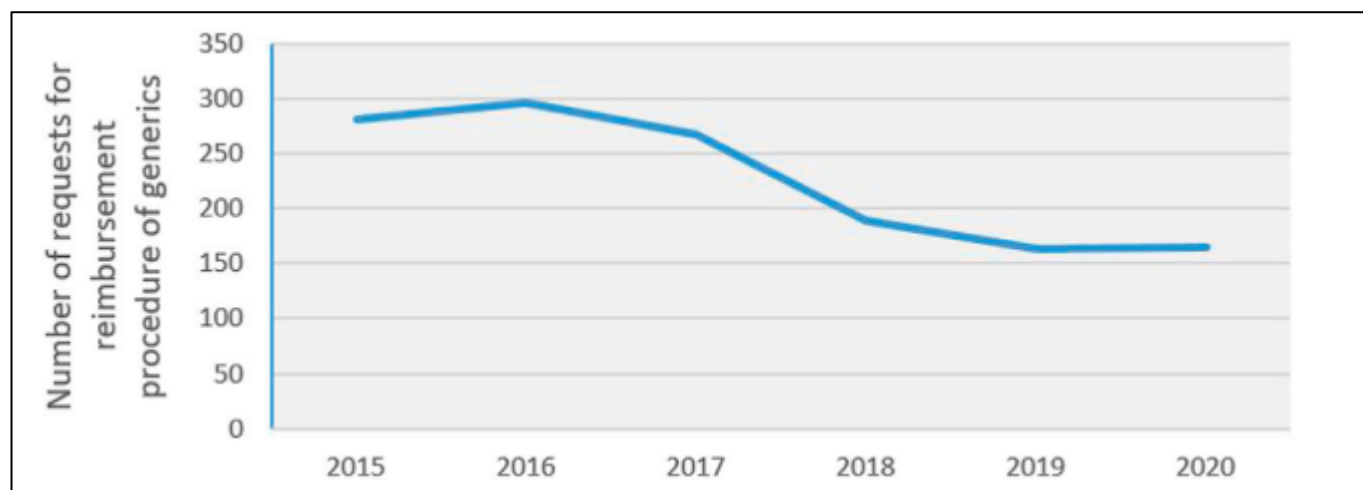
Summarising the results of the SLR update, it can be stated that the main conclusions from Puig-Junoy's 2010 review are still valid. Pricing policy tools decrease generic medicines' prices and lead to intensive price competition between manufacturers. However, price competition by high discounts to pharmacies is not passed to the consumer price. The results also show that the greater number of competitors in the market reduces the price of generic medicines.

What's more, results from the review conducted by Puig-Junoy et al. indicated that the percentage discount offered to pharmacies in a country that uses a price cap system combined with reference pricing is positively and significantly related to the number of generic competitors in the market for the pharmaceutical (dynamic price competition at ex-factory level).³⁹

Procedures and time associated with introducing a generic medicine to the market also have a large impact on limiting price competitiveness. Post-approval medicine evaluation in Slovakia takes much longer than in other countries in the region. This is the period from submitting an application for reimbursement of a generic medicine to agreeing to a maximum pricing and reimbursement from public insurance. In the case of generics in Slovakia, this period lasts on average 90-120 days. By comparison, in the Czech Republic and Hungary, this period is 60 and 30 days respectively, which is another deterrent to generic and biosimilar manufacturers and delays patients from benefiting from price competition.³⁷

Manufacturers of generic medicines who want to enter the Slovak market face several restrictions. Since January 2018 three-threshold entry has been effective, which means an obligatory reduction of prices of the first three generic medicines when entering the market. In addition to the abovementioned, there is an extended assessment period and strict conditions for external reference pricing. All of this can discourage generic manufacturers from entering the Slovak market and is reflected in data. According to the Slovak Ministry of Health, the number of applications for the reimbursement of generic medicines decreased from 296 in 2016 to 164 in 2019 (a 45% reduction over 3 years).³⁷

Figure 4. The number of applications for the reimbursement of generic medicines in Slovakia from 2015 to 2020³⁷



On the other hand, in an approximate period, sales of generics (based on DDD) increased by 5.31% between 2015 and 2020. Over the same period, generic sales fell only by 0.38% in Poland, decreased by 5.56% in Hungary, and increased by 2.23% in Czech Republic.³⁷

Figure 5. Consumption of generic medicines in % of DDD for 2015 and 2020³⁷

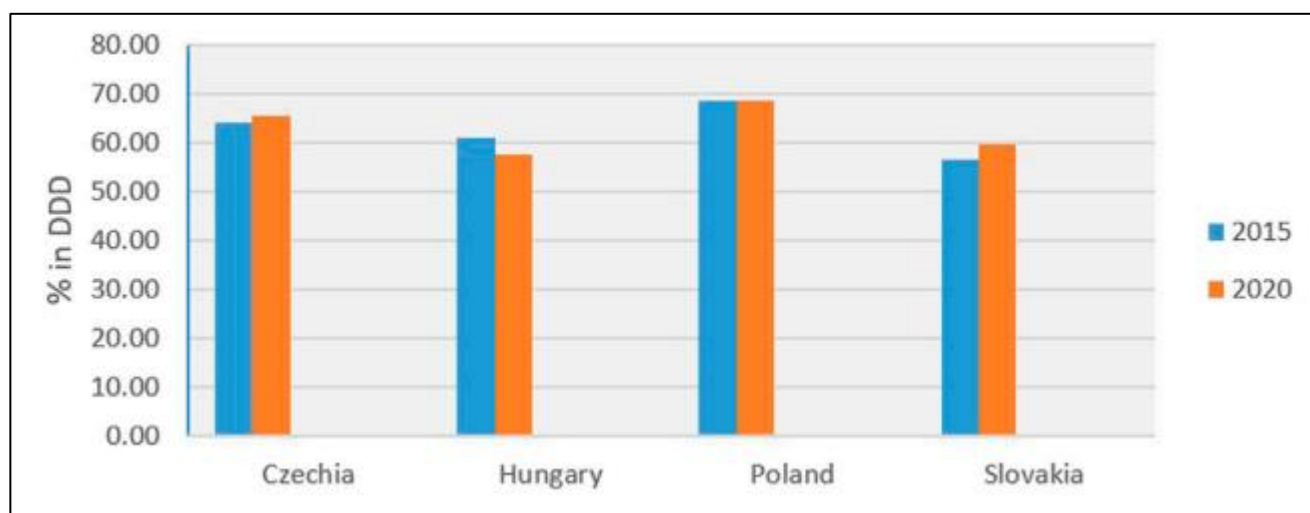
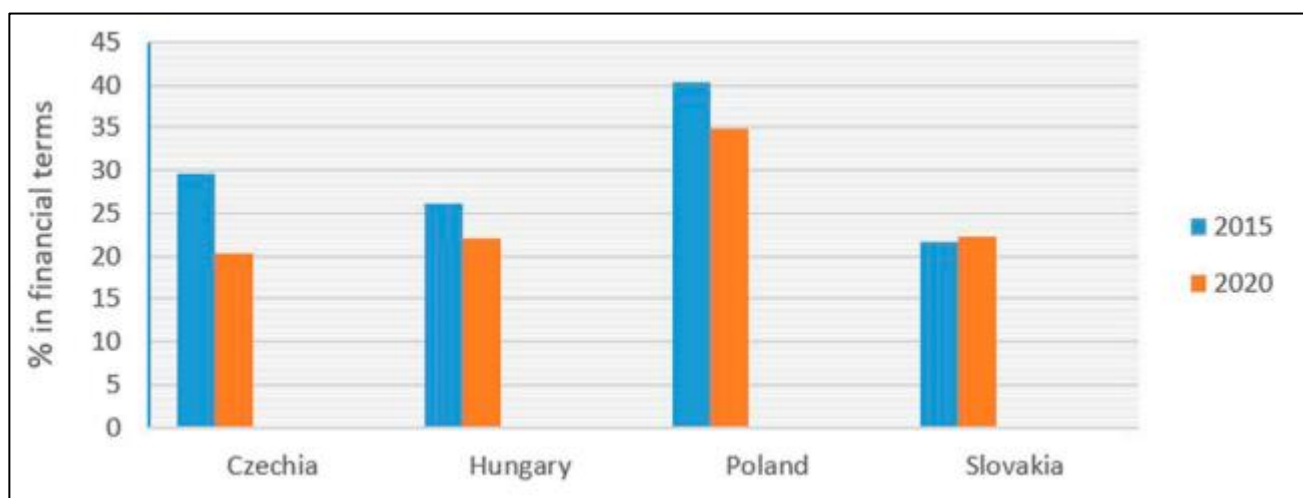


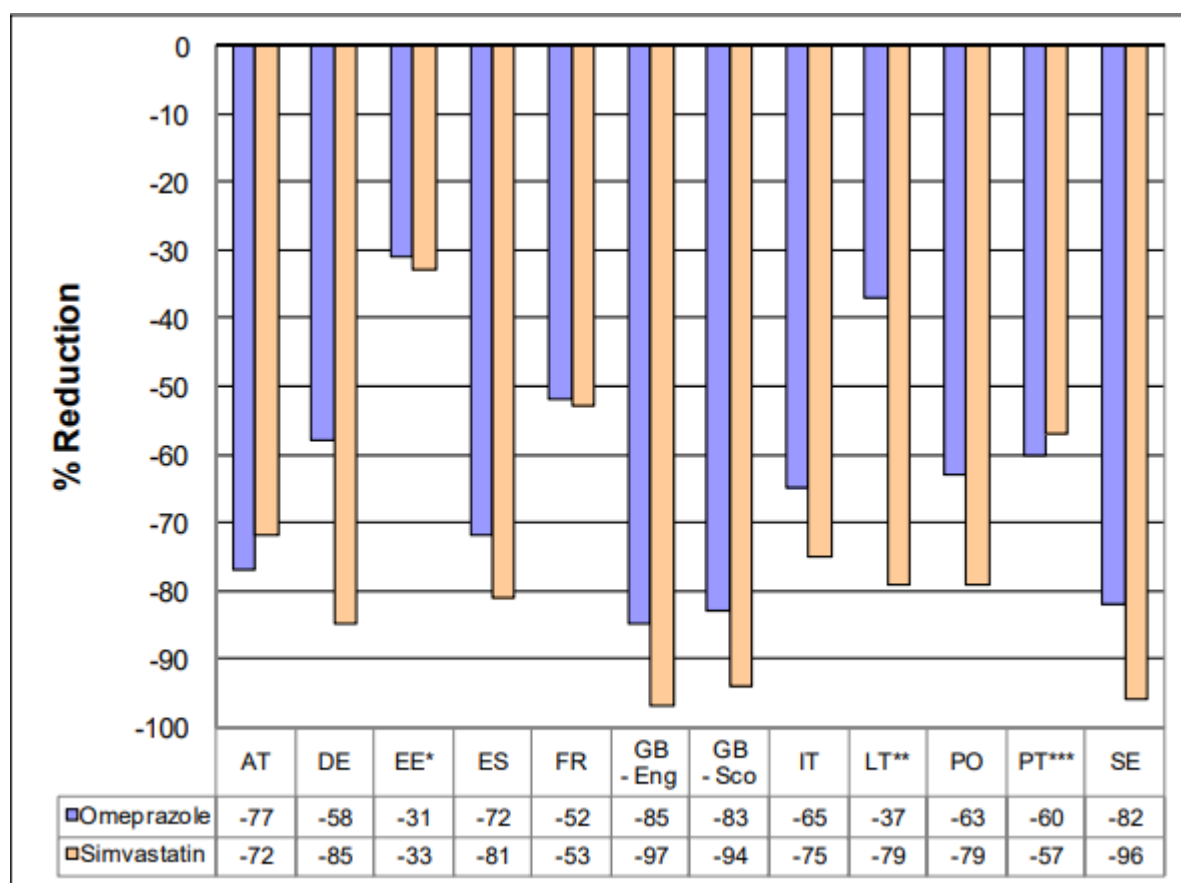
Figure 6. Consumption of generic medicines in % of financial terms for 2015 and 2020³⁷



A study conducted by Godman et al. to review additional measures that some European countries can adopt to further reduce reimbursed prices for generics, shows the impact of pricing policies on reimbursed prices of generic omeprazole and generic simvastatin.⁴²

Results from the study indicate that the various pricing policies for generics have resulted in appreciable decreases in the prices of generic omeprazole and simvastatin vs. originator prices (years 2007 vs 2001) in selected European countries (Figure 7).⁴²

Figure 7. Percentage reduction in reimbursed expenditure for generic omeprazole and generic simvastatin in 2007 vs. 2001 originator prices (unless stated) in exemplar countries⁴²



Applies to * 2004 originator, ** 2000 originator, ***2000 originator, Spain means Catalonia

Table 2 contains details of the overall impact of generic policies on utilisation and reimbursed expenditure in these two target disease areas. Only countries with an identified pricing policy impact were included.

Table 2. Impact of the various measures on the utilisation and expenditure of PPIs and statins in exemplar countries in 2007 vs. 2001⁴²

Country	Medicines	Change in utilisation (2007 vs 2001)	Change in expenditure (2007 vs 2001)	Measure
Austria	PPIs	3.6x ↑	2.1x ↑	Voluntary price reduction for single-sourced PPIs
	statins	~2.4x ↑	3% ↓	Prescribing restrictions for both atorvastatin and rosuvastatin

Country	Medicines	Change in utilisation (2007 vs 2001)	Change in expenditure (2007 vs 2001)	Measure
England	PPIs	2.3x ↑	38% ↓	Introduction of the new pricing system as well as a variety of measures to enhance the prescribing of generic omeprazole vs other PPIs
	statins	5.1x ↑	20% ↑	Introduction of the new pricing system as well as a variety of measures to enhance the prescribing of low-cost statins vs other single source statins
France	PPIs	2.1x ↑	39% ↑	Initiatives to enhance the prescribing and dispensing of generics vs originators
	statins	72% ↑	19% ↑	Initiatives to enhance the prescribing and dispensing of generics vs originators
Germany	PPIs	3.2x ↑	1.4x ↑	Introduction of reference pricing for PPIs in 2003
	statins	2.1x ↑	54% ↓	Introduction of reference pricing for statins in 2003 and the removal of atorvastatin from the normal reimbursed list
Poland	PPIs	Near doubling of the rate of increase in utilisation vs. expenditure		Reference pricing for the PPIs
	statins	4.5x difference in the rate of increase in utilisation vs. expenditure		Reference pricing for the statins
Scotland	PPIs	2.3x ↑	38% ↓	Introduction of the new pricing system as well as a variety of measures to enhance the prescribing of generic omeprazole vs other PPIs
	statins	5.1x ↑	20% ↑	Introduction of the new pricing system as well as a variety of measures to enhance the prescribing of low-cost statins vs other single source statins

PPIs – proton pump inhibitors

As presented above, countries introduced initiatives to enhance the prescribing and dispensing of generics. Another common mechanism is reference pricing. Both measures resulted in increased utilisation (improved patient access) however, expenditure was not the same in all countries.

5.3. Healthy competitiveness

5.3.1. Indicators of competition

A recent report published by OECD about methodologies to measure market competition lists two main indicators to measure market concentration:

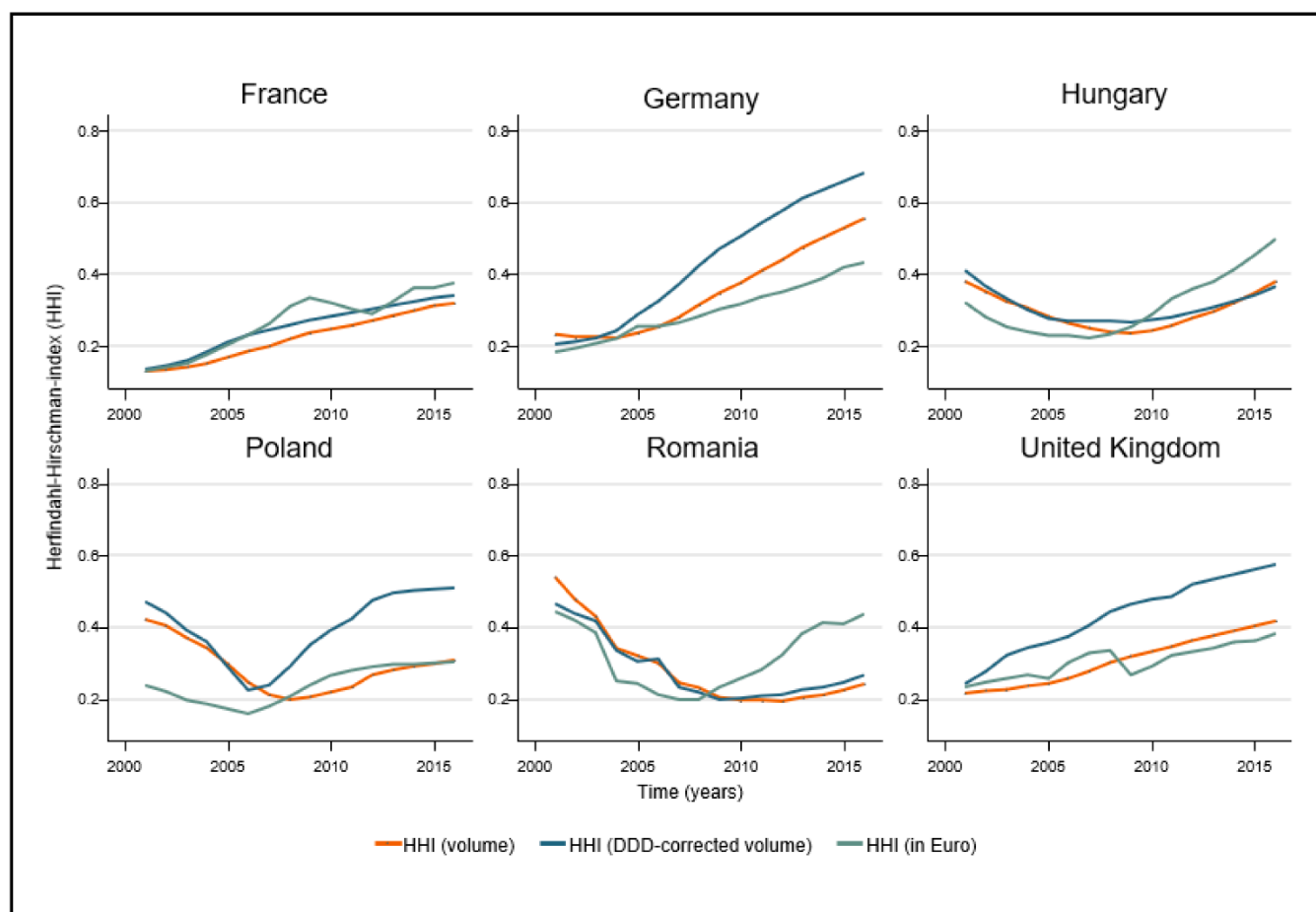
- Concentration ratios (CR),
- Herfindahl-Hirschman Index (HHI).⁴³

A concentration ratio requires information on the number of firms and the market shares of the largest firms. The N-firm concentration ratio measures the market share of the top N firms in the market. The index approaches zero for an infinite number of equally sized firms and equals 1 if the firms included in the calculation make up the entire market. Commonly used values of N include C3, C5, and C10. By focusing only on the market share of the top N firms, however, the concentration ratio takes no account of the market share distribution of the remaining firms.⁴³

The Herfindahl-Hirschman Index (HHI, also known as Herfindahl index, or sometimes HHI-score) is the most popular concentration measure in the competition literature that informs about the size of the firms in relation to the industry and is an indicator of the amount of competition among them. It is calculated as the sum of the squares of the market shares (expressed as fractions) of the companies within the industry (market). Numbers closer to 1.0 are deemed non-competitive (smaller number of players and/or concentrated market share, a single monopolistic producer), and numbers closer to 0.0 indicate a huge number of very small firms (share spread evenly across many players).⁴⁴ Increases in the Herfindahl index generally indicate a decrease in competition and an increase in market power, whereas decreases indicate the opposite or increased sustainability.

The HHI is more data-intensive than the CR as it requires information on the firm size distribution (i.e. the market shares of each firm). The HHI solves the problem with concentration ratios by summing the squares of the market shares of all firms in a market. By summing squares, the HHI stresses the importance of larger firms by assigning them greater weight than smaller ones, thus reflecting their relative size importance.⁴³ The example of using HHI to determine market concentration of ACE inhibitor active ingredients in six European countries from 2001 to 2016 is presented in Figure 8.

Figure 8. Market concentration of ACE inhibitor active ingredients in six European countries from 2001 to 2016⁹⁴



5.3.2. Impact of pricing policies on competition level

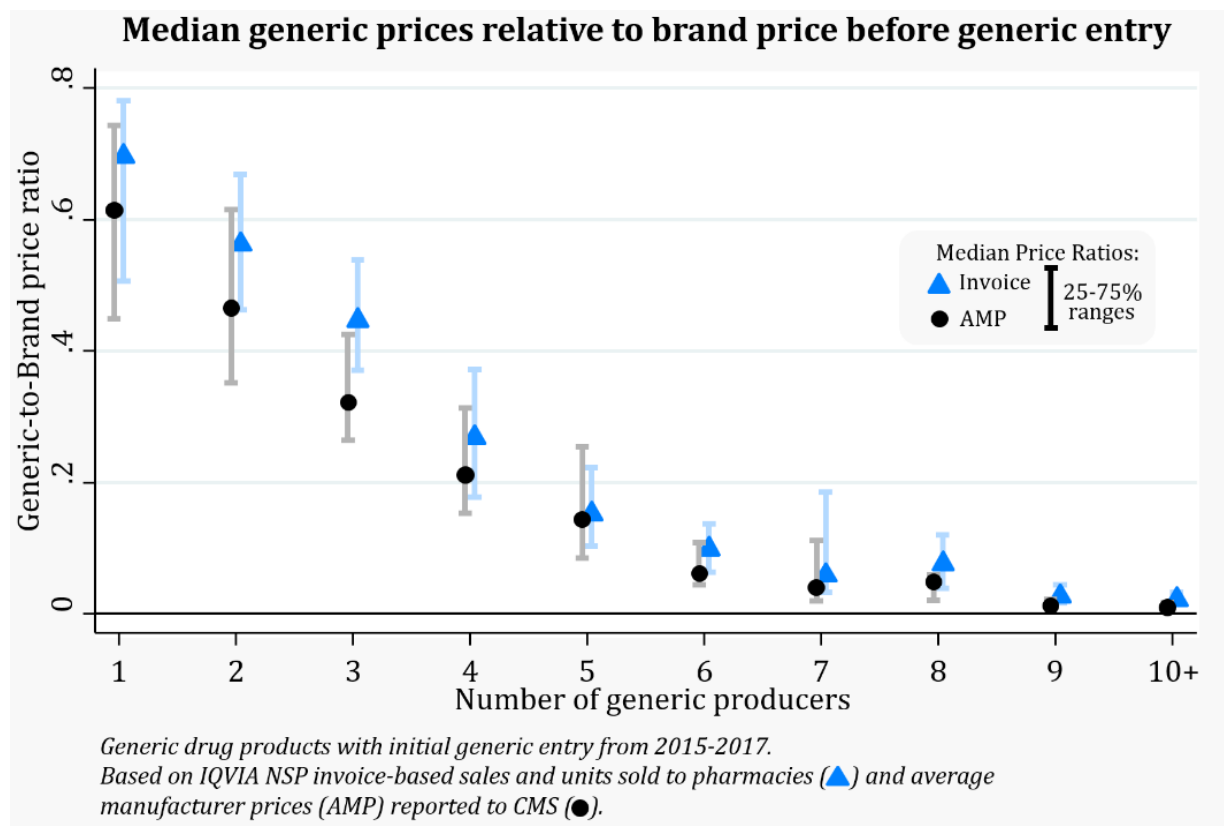
Pricing policies have a significant influence on the shape of the generic market. Mechanisms aimed at lowering medicine prices may, in the long run, have the opposite effect and increase the prices of generic medicines.

Internal reference pricing has some limitations in achieving full price competition. This is because it reduces the prices of pharmaceuticals subject to this policy to the level imposed, but without other complementary measures there is no incentive for lowering prices below the regulated price caps. Interestingly, in countries with already high generic market share, generic firms compete on prices. In these markets, free pricing appears to work better than setting price caps, as these would possibly lead to less price competition. Therefore, any measures increasing the share of generics in pharmaceutical consumption improve the conditions for price competition based on IRP but also based on free pricing.⁵ It is worth pointing out that a pricing policy is not necessarily more successful if a lower price is achieved, as this lower price can be unsustainable and lead to the withdrawal of medicines from the market.

US market is more generic-oriented than the European market and generic substitution is widely used there. The example below is to show how a change in the number of producers in the market affects a change in price. It is not possible to accurately translate these data into the European market, but similar trends can be expected.

The FDA performed an analysis of prices and competition for all drug products that had initial generic entry between 2015 and 2017, showing median generic-to-brand price ratios and their ranges by the number of generic producers.^{46,47}

Figure 9. Generic competition and drug prices⁴⁶



For products with a single generic producer, the generic AMP (Average Manufacturer Price) is 39% lower than the brand AMP before generic competition, compared to a 31% reduction using invoice prices. With two competitors, generic prices are 54% lower, compared to a 44% reduction in invoice prices. With four competitors the reductions are 79% and 73%, respectively, while with six or more competitors – both AMP and invoice prices show price reductions of more than 95% compared to brand prices. For all competition groups combined, the AMP reduction is 40% for the drugs in our sample, while the median price ratio using invoice prices is 49%.

When prices reach very low levels over time, the number of producers decreases, and prices tend to stabilise. If prices fall too low due to government cost-containment measures, markets become over-reliant on one or two producers or consolidation of the production supply chain. This increases the risk of stocks running out and a growing shortage. If prices are reduced to unsustainable levels, there is a risk of supply availability issues.⁴⁸

Generic medicine manufacturers base their revenues on sales volumes, not on margins, which are very low. Too many competitors on a market could erase those margins and prompt some manufacturers to leave. If many companies manufacture the same medicine, the price could drop so low that it is no longer profitable. If enough companies stop producing a particular medicine because of a drop in profitability, there is a risk of a medicine shortage, and a lack of competition could make it possible for an individual company to essentially become a monopoly and dramatically increase medicine prices.⁴⁹

The number of competitors for generics within the reference price system appears to be related to the extent of competition, although the impact is mainly due to discounting in the distribution chain rather than price competition. Larger discounts were seen for more generic competitors.¹⁹ A study conducted in European countries with low and high generic medicines market shares showed that the extent to which price competition from generic medicines leads to price reductions appears to vary according to the market share of generic medicines. High market share markets of generic medicines have seen a larger decrease in medicine prices than low market share markets. Countries need thus to create an environment which stimulates generic medicines use and so increases their market share.²⁴

An example from Austria shows that when the price of the third generic medicine is low, the price of the originator and also the first and second generics must drop within three months if they want to stay listed. This shows that pricing policies consisting of lowering prices of subsequent medicines may lead to their reduction significantly below the profitability level. Further price decreases are often seen down to -80% or -90% of the former starting price of the originator.⁵⁰

In a Norwegian study, reference pricing compared with other mechanisms to regulate price levels has been presented as enhancing generics competitiveness to a greater extent and leads to lower prices than price cap regulation.¹⁹

In France, generic companies struggle with a policy of cutting medicine prices. Furthermore, tax pressure and the difficulty to decrease the level of discounts are exerted on them. In such an unfavourable environment, only the largest entities with the ability to afford to reduce production costs will survive.⁵¹

In the Netherlands because of the low margin and high risks for the industry, a lot of generic medicines left the market. Since 2015, more than 3,000 generic products have left the Dutch market. For those generic products which left the market, they are coming back to the market as compounded products which are not controlled by price or reimbursement law.⁵²

The clawback mechanism allows the government to underspend on healthcare while creating an unsustainable economic environment, especially for generics companies. Extreme pricing pressures, combined with devastating clawback along with the relatively small market size, which does not allow for economies of scale, create an impossible operating environment for generics companies, which are often obliged to withdraw from the market the products that lack a viable outlook. Notably, between 2014-2019, 1,739 generics were withdrawn from the Greek market. i.e., 42.6% of all generic products present on the positive list of July 2014. During the same period, 1,232 generics were introduced, so the positive list of July 2019 includes 505 fewer generics than the 2014 list and this is a continuing trend.¹⁰

An example from Romania shows that the prices of generic medicines are set by external reference pricing at the lowest price of the twelve reference countries. Consequently, the prices in Romania are among the lowest in Europe while the cost of supplying the market is high due to a government clawback tax. This has led to the withdrawal of thousands of mostly generic medicines from the market.

The generics market in Europe is increasingly concentrated. Globally, the generics industry is growing at a rate of 12-13% (pharma growth only 2–3%), however, the number of players is declining. The mergers of the past decade have seen the market share consolidating in the hands of fewer players who typically

operate across several geographies. In Western Europe, the large acquisitions have been through Sandoz (acquisition of Hexal), Teva (acquisition of Ratiopharm, Ivax and Actavis Generics), Viatris (former Mylan, acquisition of Merck generics, Matrix, Agila, Abbott's branded generics business outside the US) and Watson (acquisition of Arrow & Actavis (and re-branding as Actavis)). The top generic companies comprising Teva, Sandoz and Viatris have cumulative revenues of \$31 billion and a market share of over 15% globally of the entire generics industry.⁵³

Examples from the US market and the assessment of the current situation in Europe indicate that the drug policy must encourage greater competition in the market of generic drugs to reduce centralisation in the market.

5.3.3. European countries policies impacting off-patent competition

The healthcare sector is one of the most sensitive regarding reaction to budget constraints and financial limitations. Greece is an example of European country that introduced austerity measures to reduce their spending on healthcare.⁵⁴ The potential for cost-containment can be observed in the context of the generic prices which may be established at a lower level (generic price linkage), and via competition intensified by the launching of a new generic to the market. The arrival of a new generic drives prices of other generics and the originator down.

Legislators and decision-makers in European countries look at the generics from a broad perspective. Some countries such as Denmark and Germany promote increased utilisation of not only generics but also “non-expensive” medicines coming from parallel import. Countries may vary greatly in the context of a price difference between a generic medicine, or other follower medicines, and the originator. It remains a question if higher price differences are possible, by how much, and whether lower prices can be achieved for generic products via policies different from the generic price linkage. The Netherlands is an example of a country where it is not mandatory to price generics below a certain percentage of the originator, and it still reports considerable price differences. It is possible due to competition on the market strengthened by the tendering system in the outpatient environment. It is proven that generics prices linkages and price regulation tools can help decrease generic prices to some extent but the competition promoting, free-pricing model is more effective in this matter.¹⁴

Besides the mentioned savings generating potential, generics play a significant role in the social justice aspect of medicines availability. Especially, in lower-income countries, the generics market entry enhances patient access to high-quality therapeutic options. To diminish substantially governments and/or third-party payers' spending, the most common practice has become setting reimbursement amounts for groups of therapeutically equivalent medicines (reference pricing). This solution, however, does not promote competition among generic manufacturers and can contribute to the shortened economic viability of a generic medicine. To gain a higher market share, the manufacturers may offer discounts or other profitable incentives directly to wholesalers or pharmacies instead of offering them to public officials or third-party payers. Payers then reimburse the full reference price. This solution leaves wholesalers and pharmacies with significant profits, while the benefits for patients (customers) and payers are minimal.

In response to this practice, some countries have enforced a ceiling on wholesalers' and pharmacies' margins or put in force profit-sharing regulations (clawbacks).²⁷ The main aim of clawback is to transfer increased pharmacies' profit to public payers' revenue.³ There is evidence that reference pricing systems or imposed, fixed discounts relative to originators are not as effective in reducing prices as competitive promoting mechanisms such as tendering or price negotiation. This does not mean that competition-inducing tools should be implemented universally in European countries. A highly customised approach should be adopted to create tailored measures that would take into consideration issues of long-term supply certainty.²⁷

At first glance, it may seem that the size of a generic market (volume) in European countries is the main predictor of generic medicines market entry intensity and generics price drop. Although significant differences in generics uptake values may be the reflection of the timing of patent expiration, generics uptake mainly depends on policies implemented at a national level. It is not sufficient though to promote competitiveness and fair pricing for generics. Encouraging rapid market entry of follow-on products immediately after the originator's loss of patent protection, mandating generic substitution and requiring INN prescribing should accompany generic market reform to generate expected outcomes. The role of physicians', pharmacists' and patients' education about generics also plays a vital role in generics uptake. In 2009 in France and in 2010 in Hungary, as part of a pay-for-performance scheme, introduced a system of incentives for doctors to increase the index of prescribed generics, with limited effect in Hungary. In Belgium, to avoid pharmacist preference toward the originator or generics the fixed fees for pharmaceutical services are set.²⁷

The existing (classic) and the new pricing models should be designed in a way that promotes off-patent competitiveness followed by the effective tools that would ensure increased uptake (generic substitution, INN prescribing). Only if those two conditions are fulfilled the economic viability of generic medicines can be enhanced.

5.4. Medicines shortages

There are multiple factors impacting the European countries' generic medicines levels of supply. Generic shortages are the manifestation of supply disturbances. The main causes of shortages can be predictable (can be controlled, modified) and unpredictable (oftentimes unprecedented, difficult to be prevented). Most of the predictable factors such as product discontinuation, industry consolidation, dynamic market shifts, just-in-time inventories, and penalties for a manufacturer that prioritises more lucrative markets, have their roots in the generic market dynamic and its potential instability. The unpredictable factors that may disrupt supplies are natural disasters, unexpected demands, epidemics, financial crises, and rapidly rising costs of manufacturing – e.g. energy costs, parallel distribution, or foreign exchange effect. The breach in the continuity of supply cannot be however narrowed down exclusively to shortages. A supply crisis should be defined as the “*a medicine/ generic medicine unavailability at the moment of its dispensing due to various reasons*”.⁵⁵

According to SPOC Network definitions and classification of different shortage root causes, commercial reasons are defined as “*Company-driven decisions linked to business aspects such as pricing negotiations; discontinuation; change in reimbursement status; low sales (i.e. low number of patients); business strategies prioritising other markets.*”⁵⁶ Data from a recent study indicate that commercial reasons were the second most common reported root cause (25%), right behind quality & manufacturing issues. What’s more, commercial reasons as a reported cause of shortages strongly increased between 2015 and 2018 up to a third (31%) of all notifications (decrease to 18% in 2020).²

According to a recent study commissioned by the European Commission, shortage notifications have increased and involve older, off-patent medicines, this is widely attributed to the low-profit margins associated with these products. Although root causes of medicines shortages are multifactorial along the entire pharmaceutical value chain, from the manufacturing of raw materials to national pricing and procurement practices, the high prevalence of localised shortages in specific markets (as opposed to the rarer EU-wide shortages) suggests that market failures are the true driver.²

Overly restrictive pricing policies may reduce access to medicines in a given country. According to causes of medicine shortages identified in the literature, an inadequate pricing policy is behind many of them.^{57,58}

A medicine pricing policy with the sole purpose of reducing pharmaceutical expenditure (e.g., reference prices or mandatory price reductions) does not allow for price adjustments to reflect changes in the cost of goods, production, regulatory procedures and / or distribution (e.g. increased cost of ingredients) and failing to provide adequate quantities have a negative impact on the reliability of the supply of medicinal products. All economic operators involved in the supply chain are directly or indirectly affected by the applicable pricing mechanisms. The profitability of these entities is critical to business continuity and supply.⁵⁸

Cost containment measures, introduced by some countries to control public expenditures on pharmaceuticals, such as external reference pricing, payback mechanisms, payment delays, etc., do not provide an incentive for industry players to continue operating in certain markets.^{58,59} The procedure that may increase the vulnerability of the pharmaceutical market to medicine shortages is price capping. In some countries, the price of generic medicines is set as a percentage below that of the original medicine. In this way, the manufacturer of the original medicine can lower its price to a point where the supply of the generic medicine is no longer financially sustainable, causing it to disappear from the market. This will lead to fewer manufacturers and ultimately to medicine shortages, especially when it comes to performance issues. Another consequence of price capping appears to be its impact on the availability of generic medicines: a European study found that price capping delays the introduction of generics compared to other pricing policy instruments.⁶⁰

Internal reference pricing may lead to medicine shortages in a similar way as external price referencing. If the price of one product drops, the price of identical or equivalent medicines will also fall. However, this procedure is used more often in reimbursement procedures than in actual pricing.⁶⁰

The most radical example of the impact of a pricing policy instrument on medicine shortages is when a manufacturer withdraws its products entirely from the market. This is because in certain conditions they

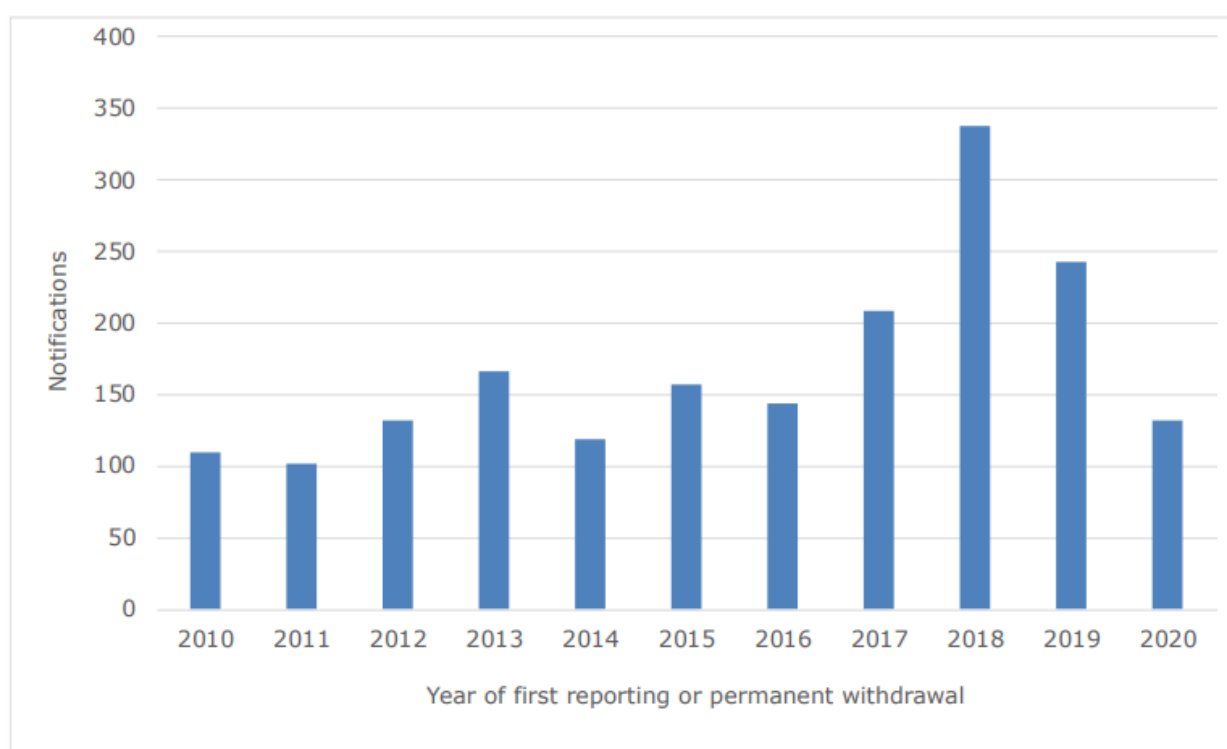
are no longer profitable. If market conditions limit the profitability of MAHs, they have no incentive to continue producing a given product and to invest more money in improving its quality.

There is strong price competition in the pharmaceutical market, also known as the "race to the bottom of prices". This practice does not incentivise MAHs to invest in the production of older generics that have little potential for returns. Essential medicines are often generics, so they are relatively cheap to buy but not easy to produce.⁶¹

Medicine shortages are a serious problem in Europe. A 2020 survey by the European Union Pharmaceutical Group among its member organisations found that all 26 countries that responded had medicines shortages in the last 12 months, and most countries (n=17, 65%) indicated that the situation has worsened compared to the previous year. In almost a third of the countries that responded (n=8, 31%), more than 400 medicines were reported as shortages. These shortages exist across therapeutic areas, including vaccines and life-saving medicines.⁶² A similar 2019 study in 39 European countries (27 EU and 12 non-EU) commissioned by the European Association of Hospital Pharmacists showed similar results, with 95% of respondents citing medicines shortages as an ongoing problem in delivering the best patient care.^{2,63}

For almost all (97%) of the medicines that were missing, the patent expired before January 1, 2021, with the median time since patent expiry being over 19 years (7,001 days).² A recent White Paper by IQVIA finds that 52%-79% of shortages involve generic products.⁶⁴ This means an increase in the share of generic drugs in medicines shortages, as previous data from a study including the years 2010-2013 indicated with 37% of reported medicine shortages being generics.^{35,65} Generic medicines remain in shortage on average for 20 days longer than non-generic medicines (125 days vs 104 days).²

Figure 10. Permanent market withdrawals over time (as reported by NCAs)²



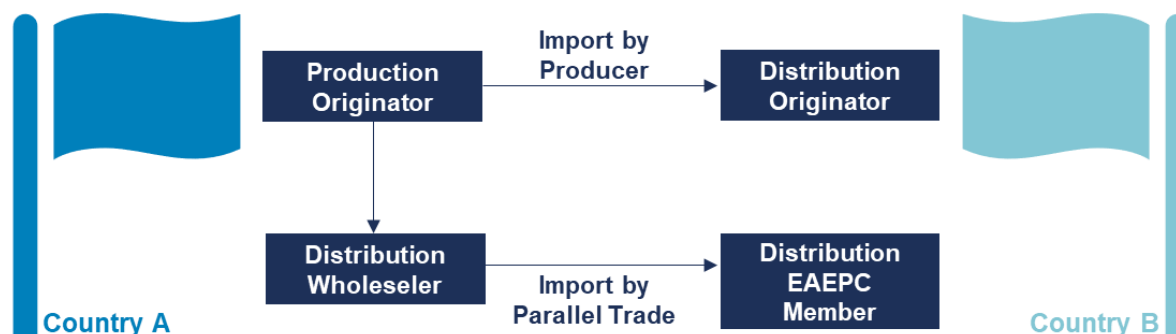
Since 2010, there has been a steady increase in the number of products annually reported as permanently withdrawn (Figure 10). Among products permanently withdrawn from the market, the primary cause of which is cited as "commercial reasons", the share of generic/biosimilars slightly rises to 54%. This finding confirms that generics are more likely to be withdrawn due to their lower profit margins.²

According to Medaxes's report about generic medicines in Belgium, 1 in 5 generics disappeared from the market in 2020-2021.⁶⁶ In the Netherlands we see the same happening since 2015 with more than 3,000 generic products having left the Dutch market. Generic products which have left the market, come back on the market as compounded products at a much higher price.

5.5. Impact of parallel trade on European price dynamics

Parallel trade is the legal practice of reselling goods between countries without the consent of the producer. In practice, a product is bought at a lower price in one country and then transported, repackaged, and resold in countries with higher prices. In the context of pharmaceutical markets, parallel distribution in the EU allows competition in areas where the pricing of medicines sold by the original manufacturer exceeds the competitive price range in comparison to other markets. This use of price differences between different national markets by parallel distributors allows consumers in all EU countries to have access to high-quality medicines at a fair and competitive cost.⁶⁷

Scheme 2. Parallel trade (adapted from EAEPC⁶⁷)



Several conditions must be met for parallel distribution to function. First, unlimited free trade between the countries involved is required. Second, there must be sufficient differences between the prices of the same goods in these countries. Otherwise, parallel distribution will be pointless. And the last requirement is that the costs of transport and subsequent repackaging must be low and competitive with the cost of the goods to make the procedure profitable.⁶⁷

Parallel trade of medicines gives patients access to safe and high-quality products at lower prices. It also impacts competitiveness which indirectly limits the increase in costs due to lower overall prices and effectively prevents original producers from inflating the prices of their products, given the monopoly situation of the patent.⁶⁷ Examples from European countries show that both generic and original medicines manufacturers increase their pharmacy purchase prices when there is no competition from parallel trade.⁹

On the other hand, parallel trade could have also a negative impact on medicines shortages. Parallel exports from Eastern Europe to Western Europe are contributing to availability problems which undermine public health. Slovakia, the Czech Republic and Romania are proposing measures to address medicines shortages caused by parallel exports: if a medicine is at risk of experiencing medicines shortages, distributors will have to notify the relevant authorities which will decide whether the medicine can be exported.²

In previous years parallel distribution of medicines occurred from “low-price” countries such as Italy or Spain/Greece to “high-price” countries such as the UK. Nowadays, almost all EEA countries are involved in parallel trade in different directions (source or destination country). The likely cause of the trend change is greater price liquidation due to complex interactions between the pharmaceutical industry and payers.⁶⁷

5.6. Impact on patient – health disparities

As shown above, pricing policies have a significant impact on the sustainability of the pharmaceutical market. Too radical a reduction in prices and declining competitiveness, in consequence, may lead to significant medicines shortages on the market.

Results of a scoping review about the impact of medication shortages on patients’ outcomes showed that medicine shortages were predominantly reported to have adverse economic, clinical and humanistic outcomes for patients. Patients were more commonly reported to have increased out of pocket costs, rates of medicine errors, adverse events, mortality, and complaints during times of shortage.⁶⁸

5.7. Key takeaways

- Supply and uptake balance to ensure continued access to medicines is crucial to ensure the long-term sustainability of the medicines market.
- Pricing policies have a significant influence on the shape of the generic market and may decrease competition level, lead to market concentration and jeopardise access to certain medicines thus increasing health disparities if applied in an unbalanced overly restrictive way.
- Without complementary measures to increase generic uptake, internal reference pricing provides no incentive to compete on prices at levels below the regulated price caps and free pricing would appear to work better.
- Several studies concluded that an increasing number of competitors led to healthy competitiveness enabling continued lowering of the prices.
- Forced price reductions may lead to such low levels of prices that impact economic viability and may lead to voluntary withdrawals from the market further decreasing competition and deepening medicines shortages.

6. Applicability of existing “classic” generic medicines pricing policy instruments to European countries

The majority of European countries that determined the cost of a generic medicine by mechanisms based on the price of the equivalent brand medicine (originator), tendering or any other variation of the reference pricing, have been experiencing an increased risk of medicines shortages. Moreover, a generic delayed market entry, in countries relying on reference pricing, entails additional significant costs for the health system caused by the later onset of generic competition and savings.²⁹ There is some evidence that tendering systems can reduce generic medicines prices in the short term, but it remains unclear how it would impact them in the longer run (potentially not a sustainable solution).⁶⁹ It can be observed that some European countries use centralised tendering or other centralised mechanisms to determine the prices of generics. The UK stands in strong opposition to tendering system introduction to primary care settings, stating that the current system even if far from ideal, minimises the scope of shortages and produces one of the lowest market prices in Europe.²⁶

Decision makers should revise existing policies whether they enable actions towards improving competitiveness (more on that in chapter 8).

The two propositions of adjusted “classic” generic medicines pricing policy instruments to enable activities towards improving competitiveness are provided below.

The first one refers to the situation in countries where no price increases are allowed and proposes introduction of negotiations on price increases. The latter proposition aims to incorporate the postulated more dynamic approach to internal reference pricing commonly used in Europe. It also assumes that both decreases and increases of reference price may take place.

Negotiations on price increases

In countries where no price increases are allowed (e.g., Portugal) it could be reasonable to provide for a possibility to make a formal submission by the manufacturer for an ex-factory price increase.

The manufacturer would need to include in the submission a justification relating to the reasons behind the requested price increase and justifying its level.

This procedure would involve negotiation meetings with authorities responsible for the decision to accept the price increase and at what level.

Such a procedure could serve as a safety valve: if several competitors for a given molecule or within a single reference group with similar, low levels of ex-factory prices submit applications for a price increase, it could serve as a yellow flag, a warning signal which identifies a group of medicines at risk of going off the market.

It would be much better for public interest and for the patients to enable submission(s) for a price increase, so that the decision-maker could see the threat incoming, assess its size and probability, and make a

decision(s) on price increases to secure continued supply of the group of medicines and maintain healthy competitiveness level.

Dynamic Internal Reference Pricing

It has been postulated by experts that internal reference pricing is a pricing policy tool that has a relatively large remaining potential.

The necessary adjustments refer to:

- (1) Calculating the Herfindahl-Hirschman Index taking into account the market shares of the reference group.
- (2) Adjusting the reference price in the group based on the value of HHI.

If the HHI decreases consistently in several measurements (which would mean that competition level consistently increases) and there is no effective competition on price, the reference price could be decreased to stimulate further competition on price. In the opposite case the reference price could be increased to provide more reward for additional competitors to enter the market.

There are similarities between this modified classic pricing policy tool to the new one discussed in Chapter 7, the tiered pricing model.

6.1. Key takeaway

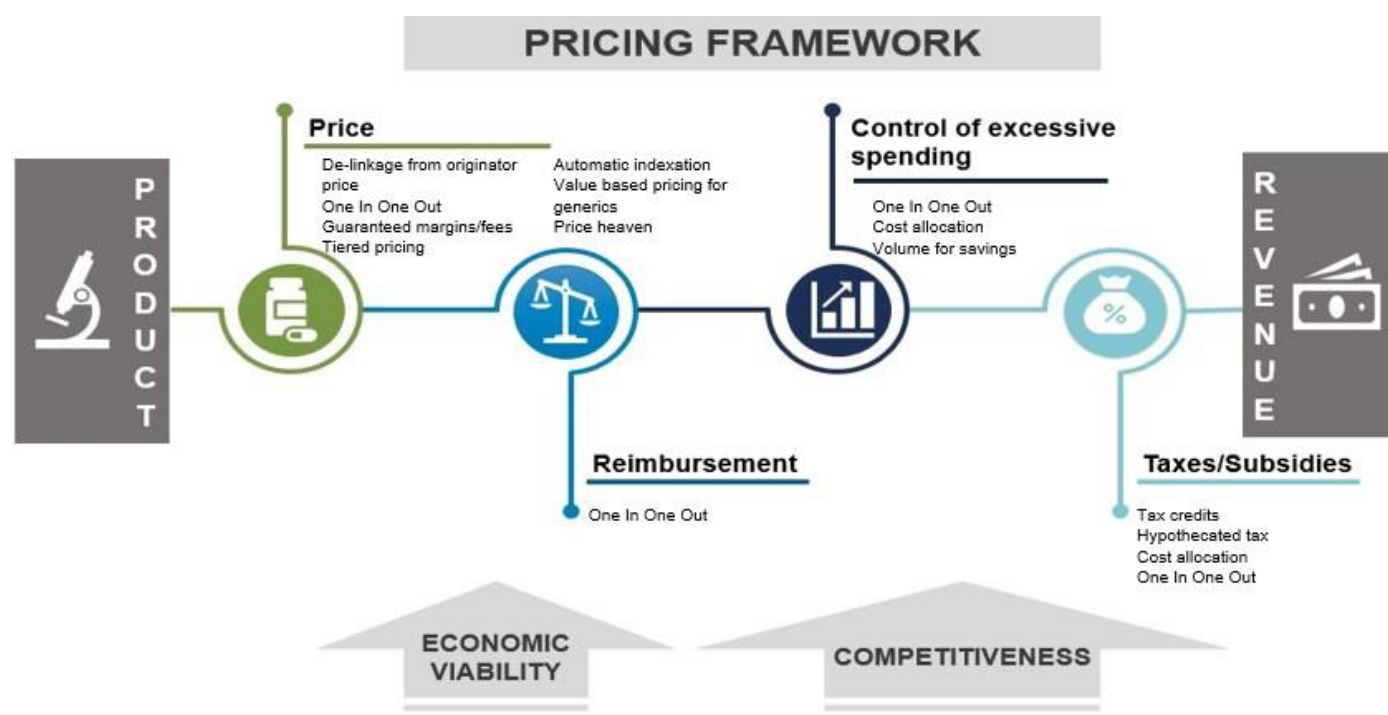
- At this point, there is no evident (clear-cut) universal approach that would balance the unsustainable generic market in Europe although decision makers should explore availability of policies towards improving competitiveness of generic medicines in their countries.
- A fundamental mindset shift is required to implement competition-sensitive approaches in policy models applied to generic medicines. New pricing policy models are adequate to address this requirement.

7. New policy models – examples from various sectors and their possible use in pharmaceutical and generic markets

As concluded in Chapter 6, at this point there is no evident (clear-cut) universal approach that would balance the generic market in Europe in the current environment. The existing “classic” pricing policies, even if they help to stabilise the generic market to some extent, seem not to be sustainable in the longer run. New pricing policy models need to be developed and explored to achieve healthy competitiveness and promote the economic viability of generic medicines in Europe. The search for new models cannot be limited to the pharmaceutical sector and should embrace an open-minded approach in the search for innovative pricing models that could be successfully implemented to the generic market.

Once a potentially applicable model has been identified, the adjustment process is necessary to tailor the selected model to the specificity of the generic market and European countries' national requirements. Rationing of medicines, generic medicines shortages, increased health risks and high societal costs are just a few examples of burdens that European countries will have to carry if they do not reform generic pricing policies. The main objective of newly developed and implemented pricing models should be the promotion of healthy competitiveness between generic manufacturers and enhancing generic medicines' economic viability.

Scheme 3. Product to revenue chain for new pricing models



New pricing policy models' predicted effectiveness to improve generic medicines sustainability were assessed. The below table with adjustments to the generic market is presented. Emphasis has been placed on the impact of a given model on the entrance to the market incentives and exit from the market prevention.

Table 3. New pricing model adjustment to generic market

NEW PRICING MODEL NAME	
Description	Short description of the main features of the model
Aim	What is the main objective of this model (what can be achieved)
Direct point of impact	What stage/ phase within the pricing framework is impacted (price, reimbursement, control of excessive spending, taxes/subsidies)
Potential for targeted use	High – if only applicable to a specific (targeted) group of medicines e.g. medicines at-risk or most commonly prescribed; Low – if universally applicable to a broad spectrum of medicines (e.g. all generics or all off-patent medicines)
Impacted stakeholders	Who is impacted negatively or positively (manufacturers, patients, authorities)
Entrance incentives	To what degree this model encourages entry into the market/sector (High, Medium, Low, No); <u>for new entrants</u>
Exit prevention / Retention incentives	How this model prevents market exit and encourages to remain on the market (High, Medium, Low, No); <u>for already existing on the market</u>
Mechanism of action	How does the model work
Possible concerns	Possible problems / objectives that may arise regarding this model

7.1. Country archetypes on generic medicines pricing policies

Countries included in the analysis are (in alphabetical order): Austria, Belgium, Bulgaria, the Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Lithuania, the Netherlands, Poland, Portugal, Romania, Slovakia, Spain, Sweden and the UK.

Countries were sorted according to similarities in their pricing framework. Five country archetypes were identified (Table 4).

Table 4. Countries archetypes

Archetype	Countries	Explanation
A1	UK, Netherlands, Denmark, Germany, Sweden	<ul style="list-style-type: none"> • Free pricing • Retail tender market for generic medicines
A2	Finland, France, Italy, Hungary, Belgium	<ul style="list-style-type: none"> • No ERP • % below originator price as main criteria to set the price of generic medicines • Clawback/ payback
A3	Portugal , Ireland	<ul style="list-style-type: none"> • Pricing mechanisms without the main objective to obtain the lowest price possible <ul style="list-style-type: none"> ○ ERP: country basket with comparable countries + average price approach ○ Clawback/ payback
A4	Austria, Spain	<ul style="list-style-type: none"> • Price alignment between the originator and the generic medicine • No clawback/ payback
A5	Bulgaria, Czech Republic, Poland, Slovakia, Romania , Greece , Lithuania	<ul style="list-style-type: none"> • Pricing mechanisms with the main objective to obtain the lowest price possible (downward price spiral) <ul style="list-style-type: none"> ○ ERP: large country basket + lowest price approach ○ Burdensome clawback/ payback ○ Price negotiations

There are three pricing policy models that stand out, among the eleven proposed models, due to their perceived high implementation potential. Tiered pricing, de-linkage from the originator price and the automatic indexation model are seen as the most feasible and effective strategies that could promote healthy competitiveness and positively impact the economic viability of generic medicines. Below, these three models are meticulously presented. The remaining eight analysed models are considered to be less effective and less feasible and are presented briefly with the possibility to be elaborated as their full description can be found in the appendix.

7.2. The Canadian pricing model for generic medicines – tiered price schedule (variation of ladder model)

Since April 2014, all generics on the Canadian market need to be compliant with the Tiered Pricing Framework (TPF) approved by the pan-Canadian Pharmaceutical Alliance (pCPA).⁷⁰

The TPF consists of three pricing tiers and applies to all generics with currently or previously available brand reference medicine (originator) that was qualified for reimbursement by any pCPA jurisdiction. The originator price is established, if possible, based on Ontario's brand reference price for all New Generic Categories, when the first generic is assessed through TPF. The set brand reference price will be used for all future assessments. The TPF is utilised to evaluate and set prices for generic medicines (to determine the appropriate price tier) that enter or exit the Canadian market. During the process of establishing price, multiple factors are considered such as the number of competitors in the market and the originator's price.⁷¹

The generic manufacturer is obliged to submit a market entry or market exit form for its product for assessment before undertaking actions leading to the product's either introduction or removal from the market.

The aim of submitting entry and exit forms is to monitor the number of generics within a Generic Category. If there is only one generic (single source of generic – one manufacturer) in a medicine category on the Canadian market it is assigned to Tier 1. If there are two generics that represent the same generic medicine category, they are both assigned to Tier 2. Analogically, if there are three or more generic, they belong to Tier 3.⁷⁰

Table 5. Tiered Pricing Framework (TPF)

Generic Medicine Category / Tier	% of Brand Reference Pricing	Notes
Tier 1: Single source (i.e. only one manufacturer of a generic medicine)	75% of brand reference price if product listing agreement (PLA) or pricing agreement for brand exists in any jurisdiction. Priced at 85% of brand reference price if PLA or pricing agreement for the brand product does not exist Maybe reassessed after 2 years following their initial assessment	Option for jurisdiction to retain PLA or pricing agreement with the brand if provides better value
Tier 2: Dual source/Two generics	50% of brand	
Tier 3: Multi-source/ Three or more generics	25% of the brand (oral solid) 35% of the brand for all dosage forms other than oral solids (e.g., liquids, patches, injectables, inhalers, etc.)	

The pCPA sets the price at 75% of the originator price for generics from Tier 1, 50% in the case of two generics in Tier 2, and 25% for generics that are in Tier 3. Probably due to more costly production, the reference prices are higher if a generic formulation is different than tablets or capsules for oral use.⁷²

It is also worth noting that TPF takes into account the source of the molecule. Even if two or more formally competing generic products have been submitted, they will all fall into tier one, if the active substance originates from the same single source. It may be explained by vulnerability to disruptions of single-source supplies. If any disruption occurs, the higher the price, the higher the probability that limited available supplies will be delivered to countries where prices are higher.

The brand reference price is established when the first generic is assessed through the TPF. This established brand reference price will be used for all future assessments. It means that any subsequent increase or decrease in the price of originator price does not have an impact on the prices of generic competitors. This is one of the forms of de-linkage from the originator's price when the relative pricing difference is kept but the originator manufacturer does not have the opportunity by lowering the price of the originator to push down prices of generics to the levels where it is no longer economically viable.

The main objective of the tiered pricing model is to establish a price based on the number of generic manufacturers ready to compete on the market within a given generic medicine category.

For Market Entrants, all competitors currently listed at higher prices must adjust their prices to match the assessed price established through the TPF during jurisdictions' next regular/scheduled formulary updates. For Market Exits all competitors currently listed will be given the opportunity to adjust their prices to match the assessed price point established through the TPF during jurisdictions' next regular/scheduled formulary updates.

This approach has the potential to automatically generate significantly low prices for high-volume competitive medicines without establishing the lowest anticipated and feasible price. It also produces higher prices to encourage generic medicines entry in situations where the competition on the market is hard to obtain.⁷³ *“Essentially, the design of the tiered pricing scheme is such that it imitates competitive pricing”.*⁷³ The more generic manufacturers supplying the market, the lower the generic price falls. With a tiered pricing model, generic manufacturers feel encouraged to enter the market as long as the price exceeds their expected average cost of production and distribution (reservation price). Manufacturers put on hold or resign completely from entering the market once the price drops to the level near the reservation price.⁷² By design, the tiered pricing system is linked to variable costs of production and distribution, so technically it should generate prices that are not remote from (close to) the efficient level. In other words, the variable cost should be between the price and the price tier immediately below. The distance between tiers can have a significant margin (in Canada it is 25% with Tier 1 – 75%, Tier 2 – 50%, and Tier 3 – 25%), so if variable costs would be 26% it is expected to have two competing oral generics manufacturers and a notable mark-up.⁷²

It remains challenging to set the price tiers in a certain manner so they can generate the lowest prices. Setting tiers close together means that to reduce the price further down it is necessary to have multiple generic market suppliers. The Canadian model with tiers far apart leaves more margins for firms but gets prices down with relatively few suppliers.⁷²

There have been some considerations in Canada regarding a potential introduction of additional lower price tiers (besides the existing 3 Tiers) that could be put into use when more than four manufacturers were willing to enter. Additionally, predictability and relative stability of the generic market could be improved in this way.⁷³

Table 6. Tiered pricing model

TIERED PRICING	
Description	The price of generic competitors depends on the reference price of the originator and the number of competitors which determines the tier for % of the reference price The reference price of the originator is set once and used for all future assessments
Aim	To promote competitiveness (incentives to enter the market), stimulate price competition, increase affordability, improve market conditions when competitors drop out of the market, slow down price decrease when it falls below the level of economic viability reflected by-products exiting the market
Direct point of impact	Price

TIERED PRICING	
Potential for targeted use	Low (high potential for general use)
Impacted stakeholders	Generic manufacturers (+) and patients (+) ("win-win")
Entrance incentives	High to medium (achievable price is higher if fewer competitors on the market)
Exit prevention / Retention incentives	High to medium (achievable price is higher if fewer competitors on the market)
Mechanism of action	Different prices based on numbers of players/suppliers on the market (number of suppliers determines a tier with a given maximum level of acceptable price)
Possible concerns	To efficiently set distances (margins) between the tiers With new competitors both the new competitors and existing generic manufacturers impacted equally negatively (need to lower the price)

Among all analysed pricing/ policy models for generic medicines, the tiered pricing model was ranked the highest as it addresses simultaneously two aspects critical for the generic market in Europe – it is adjustable to the competitiveness level and promotes sustainability. The complex nature of this model may require some specific infrastructure to be created for its successful implementation, but these investments should pay off in the future.

As the tiered pricing approach is about setting prices, it is naturally applicable in countries with already existing forms of official price setting and price capping. If implemented in countries with free pricing systems, it would apply to reference prices, especially where little or no incentives to exceed the reference price are.

- *"I'm in favour of tiered pricing so that prices might vary according to the degree of competition. Because if you have no competition, then prices will be probably higher".*
- *"This one I like. You should try to limit the amount of price regulation that you have. Anything that helps drive that flexibility in prices. With a holistic view on the demand side for generics like the UK for instance, I would support it. So according to the degree of competition, a number of players until it is competitive leave it to the market. And if it's not competitive, try to help. As a means to measure competition, I think the answer is more than three. More than three producers was a competitive market".*
- *"I think tiered pricing has the highest implementation potential, I'm very much in favour of it. I think this is a model which addresses both sustainability and the level of competition. I think it is also being applied in the United States with Medicare, Medicaid where they also have different tiers, I can see it adapted maybe to the European setting. We could do something similar, but then apply it to the reference price system."*
- *"Yes, you would need to apply it (tiered pricing model) to all of the patterns, retail medicines and yeah, and I think the only example I think it has been applied in Germany, maybe 10 or 15 years ago, they had such a system with reference prices adjusted for the level of competition."*
- *"Probably those countries that have a free pricing approach to medicines. So, Germany and a few other free-market pricing countries, yeah. But also in Belgium, where it's a regulated pricing system, we have reference groups. A manufacturer is free to set its price, and they can even set a price*

which is above the reimbursement price. But if they do so, they lose their reimbursement. So that means that in practice no manufacturer has a price which exceeds the reference price. So, I think that applies, generally speaking when you have a system of reference pricing, where there are little to no incentives to set the price above the level of the reference price. So, this model could work both in the free pricing and the regulated pricing markets.”

- *“I see it applicable in the UK, I mean the UK with its drug tariff, they have used in the past. It will make sense in countries that already do a bit of monitoring of their generic segment, by therapy area or even by active ingredient by molecule, and the number of competitors. So again, the UK is pretty good at that because the companies have to submit this information. I think in the retail market there is a lot of information on the use and margins. The issue is it is not shared.”*
- *“I think tiered pricing is a more complex system, it increases the administrative burden, and the national healthcare insurance has to follow up for each of these different molecules or markets within their country that have to collect data on the level of suppliers, prices and so on. You also have to set up an IT infrastructure. It's a very appealing model and in practice, I think all of these barriers can and should be overcome”.*

7.3. Price de-linkage from originator price

The original concept of the de-linkage model comes from the innovative medicines sector. Manufacturers of innovative medicines claim that they need to keep high prices of their products to enable R&D investments resulting in new innovative treatments. The revenue coming from sales of innovative medicines (on-patent) can be de-linked from R&D expenditures. Increasing the prices of innovative medicines is no longer a condition to ensure funds for R&D activities as alternative financial sources (direct funding – research grants, subsidies including tax credits, international research programs funds, and other financial incentives – market entry rewards, innovation inducement prizes) enable to break the link between the high price of medicines and amount of R&D financing.

There are three possible variations of the de-linkage from the originator prices model for generic medicines:

- a) **complete de-linkage from the originator price** – assumes no price capping in reference to the originator price and no forced price decrease of a generic competitor,
- b) **partial de-linkage from the originator price** – the originator price to be used as reference is established once and used in all subsequent calculations regardless of the originator's price at a given time. Any further originator price changes would not impact the prices of generic competitors.
- c) **competition maturity de-linkage** – applicable in a situation where a percentage relation of the generic competition products to the current price of the originator extends throughout the lifetime; that model assumes that de-linkage from the originator's price would take place once the competition reaches a certain level of maturity, related to the number of competitors and their market shares.

Why can the forced price decrease be a problem? Some originators abuse their dominant market position and lower their price to a level that for the obligatorily even lower-priced generic competitors proved unsustainable.

Depending on the market situation the originator price may align with generic competitors once de-linkage is introduced. The concern is if there is continued competition on prices once the relationship between the current price of the originator and of generics is not obligatory to maintain.

Arguments for the de-linkage from the originator model:

- facilitates stability and predictability of the market and provides incentives to enter the market,
- generic manufacturers can focus on competing with one another,
- the originator manufacturer either does not have any power to force lower prices for generic competitors by lowering the originator price (complete de-linkage) or loses this power when the reference price for the first generic is set (partial de-linkage) or when the market reaches a certain level of maturity.

In the context of generic medicines, the partial de-linkage model can be understood as breaking the link between the fluctuating price of the originator (used as reference) and a generic price, after the initial price (reimbursement) is established for a new generic medication entering the market.

Table 7. Partial De-Linkage from the originator price model

Partial DE-LINKAGE from originator price	
Description	Breaking the link between the fluctuating price (reference price) of the originator and a generic price.
Aim	To preserve the viability of generic competition
Direct point of impact	Price (ex-factory price)
Potential for targeted use	Low (all generics, off-patent medicines)
Impacted stakeholders	Generic manufacturers (+), off-patent medicines manufacturers (-) compared to previously privileged market position
Entrance incentives	High (predictable, sustainable market)
Exit prevention / Retention incentives	Low
Mechanism of action	Fixed internal reference price of originator ensures healthy competitiveness
Possible concerns	Not going to improve competition if it was already disrupted (for already existing groups of medicines), off-patent manufacturers' objection

Experts share the position that price linkage restrains the development of a sustainable and competitive generic market in Europe. The price linkage of generic medicines to reference medicine can significantly impact the level of market competition in two distinct ways: either by consistently forcing the prices of generic medicines to maintain a relative discount to the price of the reference medicine or by forcing the price alignment of the reference medicine to generic medicines. While the former can create situations where generic suppliers are forced to withdraw due to intense price pressure, the latter can remove the competitive price advantage of generic medicines.

The de-linkage model is ranked high in terms of feasibility as there are not many perceived barriers that would significantly impede implementation in selected countries. However, according to experts, the de-linkage from the originator model application might be limited to markets characterised by high volume and the presence of multiple generic producers. There is no healthy competitiveness associated with de-linkage from the originator price on the markets with too few generic medicines suppliers.

- *“So, these linkages at the moment are against competition. Because you're obliged to decrease prices even to the level that leads to the market exit. Generic firms reduce the price not because they have reasons to do so, but because they are obliged to do so.”*
- *“Market should resemble a competitive market. And to resemble a competitive market means that you should try to limit the amount of price regulation that you have. So, eliminate linkage and there will be price flexibility”*
- *“I think that is probably the easiest measure to implement among the set of measures that you are proposing. De-linkage makes sense according to the level of competition that you have in a certain market”.*
- *“I think such a model could only be applied to countries or to molecules with a large volume. The fact that there won't be much competition and if you only have one or two suppliers in the market, we know that competition will not happen”.*

7.4. Automatic indexation

As the COVID-19 pandemic and war in Ukraine are leading to an increasing inflation rate worldwide, it may become more acceptable to consider taking into account automatic indexation models when discussing prices of generic medicines. Currently, the increase in cost of goods and the mounting inflation cannot be reflected in the price of medicines, as these are highly regulated.

Automatic indexation models assume that a value impacted and eroded by inflation will be protected against such impact with automatic adjustment based on fluctuations in the prices of goods.

An example could be the **automatic indexation of wages and pensions** in Luxembourg and Belgium, which was designed to prevent the loss of purchasing power of consumers due to inflation. Inflation is measured using consumer price indices (CPIs). For Luxembourg, these CPIs are calculated by the National Institute of Statistics and Economic Studies, STATEC, with data on ca. 8,000 prices collected from the first two weeks of every month. If the average of the previous six months reaches or exceeds a certain rate, it will trigger an automatic adjustment of wages and pensions by 2.5%. The most recent adjustment took place in April 2022.⁸⁹ The workers and pensioners perceive it as a valuable social benefit which attracts people from abroad, but some companies see it as an obstacle to staying competitive.

The first example related to the healthcare sector comes from Canada, where the Patented Medicines Prices Review Board publishes annually the **CPI-Adjustment Factors for patented drug products** for a given year.⁹⁰

Table 8. Example of CPI-Based Price-Adjustment factors for 2022⁹⁰

Benchmark Year	2019	2020	2021
Price-Adjustment Factor	1.050	1.027	1.007

These factors for 2022 are based on the actual rate of CPI inflation of 2.3% in 2018, 2.0% in 2019, and 0.7% in 2020.

The value of the CPI factor for 2019 (1.050) means that the maximum allowable cumulative price increase is equal to 5.0% between 2019 and 2022 for patented medicines with Canadian sales in 2019. Analogically the value of 1.027 for 2020 allows for a cumulative price increase of 2.7% between 2020 and 2022 unless the patented medicine was not sold in Canada in 2020. The year-over-year price increase cap for the 12-month period ending December 2022 is 1.1%, which is equal to 1.5 times the actual inflation in 2020.

The method concerns patented medicines only and index values to be used to adjust prices in the next year (2022 in this instance) are announced in the current year (Dec 2021 in this instance). Despite that in Dec 2021 the actual inflation rate available is for 2020, the regulation provides for the calculation of the rate applicable for the whole year of 2022, which equals 1.5 times the actual inflation rate in 2020.

Another proposition is adjusting the prices of medicines by changes in the **producer price index (PPI)**. According to the OECD, PPI “*measures the rate of change in prices of products sold as they leave the producer. It excludes any taxes, transport and trade margins that the purchaser may have to pay. PPI provides measures of average movements of prices received by the producers of various commodities. It is often seen as an advanced indicator of price changes throughout the economy, including changes in the prices of consumer goods and services.*”⁹¹

Germany has a specific inflation adjustment regulation that allows it to adjust the so-called price moratorium (a price freeze instrument in reference price free market Rx segments) for the **yearly inflation index**. Even though the idea behind it is good, it has had less effect than hoped in the highly regulated German drug price regulation environment due to conflicting mechanisms.⁹²

The yearly inflation index in Germany applies to all off-patent drugs and the amount of compensation (the rise of the price cap) is as high as the latest official inflation index (Verbraucherpreisindex).

The mechanism is applied once a year as it works with the index value of the last year. Therefore, the method is retrospective and quite slow – a fast increase of inflation as we have now due to the war cannot be handled.

Another proposition related to the concept of automatic indexation is a **Regulatory Cost Index model**, which assumes that the value of the index reflecting a level of regulatory burden is recorded at the moment of market entry of a given medicine with a given price. If the regulatory burden changes with a new regulation, the value of the index will be adjusted arbitrarily, and the price of the medicine will also be adjusted using the new index value.

All automatic indexation models are perceived as a way of shifting the whole risk of inflation (or increasing regulatory demands) from manufacturers to the public payer. It would be the case if they were based on the whole inflation rate being taken into price adjustment. In such a case acceptability of these models is not expected to be high.

Nevertheless, to increase acceptability one could assume that negotiations and a sort of risk-sharing could be implemented between manufacturers and public payers – instead of medicine prices being adjusted for the whole inflation rate they could be adjusted for a fraction of it (e.g., half) in order to secure agreement.

As for the regulatory cost index model the fundamental challenge impeding its acceptability remains in its purely arbitrary nature as there is no model to quantitatively reflect the change in regulatory requirements in the new value of the index.

7.5. One-In-One-Out (OIOO)

In a democratic world, there is a strong desire to reduce and consolidate the costs related to existing and new legislation. The newer regulations are introduced on the top of the existing ones, the higher the financial burden. Not only the financial aspect is concerning due to multiple regulations in place. Over-regulation (red tape) of a market negatively impacts competition. It is visible in many sectors, pharmaceutical included.⁷⁴ *“We must have more competition and less red tape in pharmaceuticals – the sector is too important to the health and finances of Europe’s citizens and governments to accept anything less than the best”* – said European Competition Commissioner Kroes.⁷⁵

The President of the European Commission – Ursula von der Leyen – has picked the “one-in-one-out” (OIOO) approach to be the dominant strategy for the European Union policy from 2022 onwards (currently there is a pilot program going on). The EU wants to compensate (balance) the burdens and consequences occurring as the result of the Commission’s legislative proposals with an equivalent reduction of burdens already existing in the same policy area.

The main objective of the OIOO is to alleviate an old regulation (One-out)⁷⁶ when a new regulation is implemented (One-in) to achieve a neutral effect and avoid over-regulation, cost accumulations, and excessive bureaucracy. Typically, the most irrelevant or obsolete regulation is removed while the new one is implemented. The regulation replacement process should be carried out based on in-depth case-by-case analysis and assessment not according to the bookkeeping approach. The “mechanical” replacement is strongly criticised.⁷⁴

If multiple regulations are to be wiped out, the OIOO classic approach transforms into the one-in-x-out (OIXO).

The European Commission adopted three types of arrangements to simplify the process of OIOO introduction and to make the whole system more dynamic:

- Flexibility: in terms of the reporting period (if the “out” is not possible to be identified along with “in”, it can be identified and reported the year after the year of the initial program)

- Trading: if it is difficult to identify “out” within the same policy area, the Commission may decide to pick the “out” from a different policy area
- Exemptions: (only under exceptional conditions) if there is political pressure to regulate, but the alleviation (an offset) is hard to pinpoint, the Commission can decide on regulation exemption

7.5.1. OIOO/ OIXO for generics

OIOO in regard to generic manufacturers can be a method to remind decision-makers and legislators of the growing imbalance between the regulatory and other costs which generic manufacturers have to bear, and their diminishing returns due to stringent pricing policies. This way it can reduce the further negative cost impact on the generic market and thus help to facilitate generic medicines' undisrupted supply (shortages prevention). Loosening the red tape around the tightly regulated generic market in some of the European countries may support sector stability and boost its profit margins. The OIOO model presents potential prospects for increasing generic medicines' economic viability due to its close to neutral impact on additional costs.⁷⁷

In practice, if the new regulation is introduced and it entails increased operational costs for generic manufacturers it is essential to provide an opportunity for manufacturers to compensate for rising costs. Generic medicines manufacturers operate already on minimal margins, so the detrimental effect of growing operational costs should be balanced by introducing adjustments to pricing policies to improve returns. All possible measures should be undertaken to promote healthy competitiveness and to reduce the risk of generic manufacturers' withdrawal from the market due to increased costs and lack of economic viability.

Table 9. One In One (X) Out model

ONE IN ONE (X) OUT modification for generic manufacturers “Before considering any new regulatory burden on generic manufacturers, note there is an intensifying imbalance between growing costs they have to cover and their diminishing returns due to restrictive pricing policies”	
Description	A method to remind legislators and decision-makers that generic manufacturers already bear the financial burden of various regulations coupled with diminishing revenues arising from current restrictive pricing policies Label to make certain legislative changes more acceptable by stakeholders („stick and carrot” approach) OIOO suggests keeping the current balance of regulations OIXO suggests that the burden of regulation be decreased for all generic manufacturers
Aim	Should be used as a label to stick to a comprehensive legislative proposition To alleviate the negative impact or burden of the excessive number of regulations, to promote competitiveness
Direct point of impact	Potential points in product to revenue chain (universal approach)
Potential for targeted use	Depending on the selection of regulations to be introduced and removed
Impacted stakeholders	Manufacturers (+), authorities (+)

ONE IN ONE (X) OUT modification for generic manufacturers
“Before considering any new regulatory burden on generic manufacturers, note there is an intensifying imbalance between growing costs they have to cover and their diminishing returns due to restrictive pricing policies”

Entrance incentives	Depending on the selection of regulations to be introduced and removed
Exit prevention / Retention incentives	Depending on the selection of regulations to be introduced and removed
Mechanism of action	New regulations “ins” replace “outs” – “offsetting”, cutting the “red tape”
Possible concerns	Lack of specificity, in-depth analysis required prior to offsetting (replacement) Requires the careful selection and multiplying of regulations to be removed, oriented towards addressing expectations of important stakeholders

Experts do not consider the one in one out (OIOO) as a pricing model *per se* but rather as an overarching concept, an additional tool that can be used to “cut the red tape” and reduce bureaucracy. The administrative and financial burden may deter generic manufacturers from entering the market and increase the costs of production. Simplification of procedures might be a first step towards enhancing generic medicines' market viability and competition. As OIOO is not a specific tool that would enable prediction of certain implications, it is difficult to envision how it would work in practice and what implementation strategy should be used for its introduction to European markets.

- *“Administrative burden...what they could do to reduce is, for example, you know that in Europe, countries have 180 days to decide about pricing and reimbursement of new medicines. Why don't they reduce it to 0 [or just a few] days?”*
- *"It looks really great in theory...in practice, I'm not that sure. We are all aiming to, let's say, simplify procedures."*
- *"I fully agree with the principle one in one out to reduce the administrative burden. I fully support that but I'm a bit sceptical about whether this will happen in practice. If you look at regulation and the administrative burden related to generic medicines that only increases over time."*
- *“We have to distinguish between regulation and bureaucracy. We have to avoid bureaucracy. The problems related to bureaucracy and under the table payments and all this underground economy. It's a very naive approach to say one in one out. If you take one regulation, you may have to exclude two or three.”*

7.6. Tax credits

Governments do their best to incentivise industry sectors that are critical for their economies and social well-being. Tax credits are one of the incentivising tools that help to minimise taxes for strategic manufacturers or entities. The research and development (R&D) sector in the US is constantly supported and rewarded by the government due to its investments in research. In 2015 the PATH Act permanently expanded R&D sector tax credits.⁷⁸

The generic manufacturers, who despite noticeable obstacles and struggles related to operating on almost negative margins, should also be considered as strategically important (providing the affordable

therapeutic alternatives for expensive innovative medicines) for the European economy and the Europeans' well-being. Generic medicines manufacturers could be offered tax credits in return for their intensive effort to remain on the market and compete.⁷⁷ Similarly, the R&D sector struggles with extremely rapid technological changes that impose an uninterrupted and urgent need to innovate, which entails significantly increased operational costs. Also, there is an analogy between generic medicines and the R&D sector in terms of raising costs that often lead to market exit and no return.⁷⁸

Tax credits for R&D were introduced in the US in 1981 as a two-year incentive program and have proven to be effective enough to become an inseparable part of the tax code until today. Tax credits are available also for R&D taxpayers that have increased the quality, performance, reliability or functionality of their products or processes. If the development regards internal-use software (IUS) there are three conditions that must be fulfilled:

- the product must be innovative,
- the process of product development is related to significant economic risk and/or uncertainty,
- a similar product is not available.

7.6.1. Tax credits for generics

Tax credits for generics in Europe are especially considered for manufacturers who market at-risk-medicines. The term at-risk-medicines (medicines whose economic viability is under tangible threat) refers to medicines whose profit margins are very low, almost not profitable and there is a high risk of their shortages. Thus, there are no incentives for producers to continue to allocate their resources to those products' marketing. To introduce tax credits, an agreement between authorities and generic companies needs to be achieved in terms of certain conditions (for example Key Performance Indicators – KPIs) that would allow classification of a given medicine as an at-risk-medication. Possibly, companies which despite obvious disadvantages and costs decide to bring back at-risk-medicines to the market to the required supply level would be granted tax credits that translate into a tax reduction.⁷⁷

It seems that the tax-credits approach can provide some level of flexibility and adjustment towards dynamic market changes. If certain medication viability will be negatively impacted, a manufacturer whose profit margins fall drastically could request potential support in the form of tax credits prior to a decision to leave the market. Additionally, it is believed that this model can promote competitiveness and even bring back some former competitors due to obvious incentives.

As tax credits are not a unified and highly universal approach, the potential challenge arises at the moment of determining the right amount of tax credits that should be distributed. The amount may vary greatly depending on the medicine; each case needs to be analysed separately. This creates an additional demand for human resources that are qualified to do so. Additionally, there might be a polarity within European countries regarding tax credits based on the general attitude to generics. Not all countries may view the generic market as the key, strategic sector and thus not be willing to offer tax relief packages.

Table 10. Stay & Deliver Tax Credits model

STAY&DELIVER TAX CREDITS	
Description	Tax credits are given to manufacturers (already operating on the market) as a tax relief measure to encourage them to continue supplying at-risk generics to previously agreed supply level – “stay and deliver”
Aim	To ensure continuity of supply of at-risk and potentially at-risk medicines (generics) and to prolong economic viability of at-risk generics
Direct point of impact	Taxes / Subsidies
Potential for targeted use	High (at-risk medicines, potentially at-risk medicines)
Impacted stakeholders	Manufacturers of (potentially) at-risk medicines (+)
Entrance incentives	No incentives
Exit prevention / Retention incentives	High
Mechanism of action	Tax relief for continuing supply despite the significant economic risk (uncertainty)
Possible concerns	Relation between tax relief amount to the value of agreed supply level, the potential for unequal treatment by authorities, the potential for the differing significance of tax credits to manufacturers with different portfolios, immediate tax relief (right after supply agreement) vs postponed relief

Experts pointed out that pricing models like tax credits that interfere with national taxation systems may raise questions about their legality or compliance with already existing tax arrangements. The general idea of providing financial support to generic manufacturers has a positive review, but not in the form of tax credits. Conflict of interest, lack of transparency, accusations of unequal treatment, low political support, and difficulties to envision the process of implementation are the main obstacles that significantly decrease the tax credits' potential to be introduced to the generic market.

- *"I don't know if it's legally possible, in our European taxation systems (different tax arrangements)"*
- *"I like the least and that I think also it might be more difficult to gain a political support for this is the tax credits". "The tax credit is going beyond the pharma and the drugs problem. Tax credit might be difficult and might not achieve the goal because it's taken just as an opportunity...no reason to believe that these tax credits will be used for investment."*
- *"When you give tax credits to generic companies, what would be the reaction of the originator company? if you would do that in Belgium, they would file a lawsuit because it does not create a level playing field."*
- *"I would be in favour of having tax credits, but they should apply both to the generic and originated company. In reality, as you know, most companies have both innovative and generic products, so this division is not relevant anymore."*
- *"I think there are opportunities within the European legislation to have some level of discrimination for a temporary time in order to avoid, for example, shortages as a public health crisis, but then"*

you need to reflect on the legal provisions and the European legislation on how and to what extent you can accommodate for this."

7.7. Cost allocation

The cost allocation model, as its name may suggest, causes the allocation of costs to multiple, different stakeholders within the supply chain according to their contributions and responsibilities in the process. Allocation of cost regarding public goods or regulations with collective population responsibility is often transferred to end-users in the form of user fees.⁷⁷ It is a common practice to allocate costs in a proportional manner accordingly to the share of responsibilities. This approach is highly criticised due to not considering the heterogeneity in the costs imposed on different stakeholders. The stakeholders within the supply chain who carry costs higher than they can achieve independently are likely to move away from the collective system. Without collective unity of the system that maximises cost efficiency, there is a fragmented system with a higher total cost.⁸¹

The end-user fee (patient fee) would consist of a fixed monetary amount added to the medicine's standard market price for a patient. The additional patient's fee (distributed fairly across the users) set by the government helps to ensure access to medicines and enables generics manufacturers to continue marketing due to financial burdens. The authorities are responsible for proper cost allocation arrangements thus the cost coming from the fee is distributed directly to relevant entities. Ultimately, patients as co-responsible for medicines disposal would get secured access to their medicines at a higher cost.⁷⁷

Table 11. Cost allocation model

COST ALLOCATION	
Description	To compensate for rising operation costs of generics production all involved in the distribution chain (wholesalers, pharmacies) so that patients would be co-responsible for cost-sharing in the name of "common, greater good" – guaranteed supply of medicines at-risk of shortages. The third-party (independent entity) would be established to transfer gathered funds to at-risk generic manufacturers.
Aim	To cover the increased operational cost that medicines suppliers have to cover on their own, to secure medicines supply
Direct point of impact	Collection stage: Prices Redistribution stage: Taxes / Subsidies
Potential for targeted use	Collection stage: No (permanent fee applied to a group of medicines/products, not applicable directly to medicines at-risk) Redistribution stage: High (to manufacturers of medicines at-risk)
Impacted stakeholders	Manufacturers of at-risk medicines (+) and patients (-/+) (patient fee), other manufacturers, wholesalers and pharmacies (-)
Entrance incentives	Low
Exit prevention / Retention incentives	High

COST ALLOCATION

Mechanism of action	Fair distribution of costs within the distribution chain (resulting in practice in end-user fee)
Possible concerns	<p>Patients' objections to additional costs</p> <p>Compared to simple ex-factory price increase cost allocation seems to be overcomplicated, inefficient and non-transparent (involves the arbitrary redistribution of gathered funds to generic manufacturers)</p> <p>Unnecessary circumvention of simple application of higher ex-factory price, the gathered funds will be shorter of acquisition and redistribution costs</p>

All pricing models for generics that require additional patients' co-payment (hypothecated tax, cost allocation or other types of cost-plus model) have uniformly been appraised by experts as having a very low implementation potential. There may be some European countries (Denmark, Sweden or Norway) that due to their long-standing tradition of collective responsibility and common, public good, could possibly consider the implementation of a pricing policy model that requires an additional end-user (patient) fee. However, in the vast majority of European countries, the strong objection of decision-makers and patients is expected as there is no social acceptance of extra payments, even the symbolic ones. Additionally, the financial burden associated with a medication purchase stands in opposition to the idea of social justice and can contribute to deepening social inequalities related to access to affordable healthcare.

- *"All these payments and co-payments for drugs brought a tremendous financial burden"*
- *"Hypothecated tax is probably applicable in Denmark or Sweden or Norway. In Central and Eastern Europe, we hate the concept of collective property."*
- *"You will not be able to convince politicians and decision-makers that they have to announce on television that from tomorrow onwards, all patients will need to pay an additional co-payment because we consider healthcare to be a public good. And they would argue look, we already pay through our taxes for healthcare and there is just no rationale for increasing prices."*
- *"Increased prices create some sort of increasing health inequalities and we have measured and analysed health inequalities in access to medicines. They increased with out-of-pocket payments and then we have carried out also some analysis on the relating the out-of-pocket payments with the catastrophic effects."*

7.8. Guaranteed margins/Guaranteed fee

The guaranteed margins/ fee model sets a minimum profit (remuneration) for a generics manufacturer. The decision-makers at the national level determine the monetary value needed (profit/margin) to support manufacturers and ensure the supply of at-risk-medicines. A guaranteed margin/fee approach needs to set a fee sufficiently above the price of production and distribution to ensure a profit that would cover the marketing costs of certain medicines in a sustainable manner. Besides being supported by guaranteed fees, at-risk-medications should not be subject to additional price cuts that might be applied to the pharmaceutical market. The height of the fee or the level of the margin mostly depends on the characteristic and complexity of the manufacturing process as well as the prices of the standard medicines in different European countries. It seems reasonable that each country establishes guaranteed fees (along

with fee indexation) based on a domestic proxy or by exploring the operating price levels of the local pharmaceutical market. Guaranteed fees can be adjusted to the current market situation and thus shows resilience towards unexpected disturbances.⁷⁷

Table 12. Guaranteed margins / fee model

GUARANTEED MARGINS / FEE	
Description	A direct link between the cost of production/distribution and ex-factory price, 1) manufacturer discloses production/distribution cost 2) authorities set the margins/ fees per pack in tiers inversely proportional to the number of competitors 3) newly established ex-factory price 4) costs review in reaction to macroeconomic changes (cost increase) or change in the number of competitors or at pre-specified intervals 5) tiered margins/fees review in reaction to effectiveness in stimulating competition (market-regulatory feedback loop)
Aim	To promote competitiveness (incentives to enter the market), to increase affordability
Direct point of impact	Price
Potential for targeted use	High (high cost of the operational implementation of regulation limits its use to at-risk medicines)
Impacted stakeholders	Manufacturers of at-risk medicines (+), patients (+/-)
Entrance incentives	Medium (dependent on the pace of decreasing the margin/fee along with the decreasing number of competitors)
Exit prevention / Retention incentives	High
Mechanism of action	Different prices based on numbers of players/suppliers on the market (number of suppliers determines a tier)
Possible concerns	To efficiently set distances (margins) between the nearby tiers and the number of tiers Methods to deal with differences in submitted costs of production/distribution among the competitors

The main issue regarding the guaranteed margin/fee model is the inability to calculate the exact cost. Not only the willingness of producers to disclose the accurate cost might be problematic but also the ability to do so. Production and distribution costs are just a fraction of the total cost. Besides the obvious problem with cost verification, there is also the concern regarding transparency and trust that appears in a couple of dimensions. It seems that economic viability of generic medicines might improve due to introduction of guaranteed margins/ fees, but it is not a long-lasting, sustainable strategy. This model as the stand-alone concept does not provide enough incentives for generic producers, it is suggested that it should be combined with other tools to bolster competition.

- *“If we have a low number of competitors, we may expect the price to be higher. The price increases but is there the possibility to really enter the market if production costs are also high. So, you try to ensure the margin, guaranteeing a fee to the producer for this market entry. How do you measure the cost? How do you ensure that pharmaceutical companies are reliable in producing cost figures? How do we monitor that? So, this is a major issue that I have. I must confess that I don't have a real answer for that”.*

- *“I think this pricing model addresses the concerns of the generic industry in terms of economic viability at guarantees that or supports that. However, I think we need to supplement it once again with incentives for competition because I don't see any incentives within this model. And I share the concerns about operationalizing. Manufacturers would need to disclose some cost data and that is always a very sensitive issue.”*
- *“Besides what has been said about cost, I would like to add the issue of trust, and political vulnerability. Having the history in mind it would be pretty hard to reach an agreement within the government regarding the way how to regulate those margins and fees. To me, this is pretty much a political decision about the way that we regulate, pricing for mass pharmaceutical in Romania”.*
- *“Conceptually, I tend to be against any kind of cost-plus type of regulation for pricing because it doesn't provide the right incentives to reduce costs, letting alone all the complexities about measuring cost. Generic producers are OK at least maybe in the short term because you ensure this viability by ensuring a profit margin for the first two or three years, and then you leave it to the market or something along those lines. Conceptually any cost-plus type of regulation for pricing should be avoided or not used very often”.*
- *“First of all, what about cost? What about the measurement of cost? The first question is what about the cost components? Is it the short-term cost, the immediate cost of production or the longer-term cost and then coming back to economics, is it average cost pricing or marginal cost pricing and is this related to the market structure? But what about transparency? It was mentioned. Are we aware of the facts that the pharmaceutical industry will be willing to present the cost and what is really generated out of this and what cost component they would really try to hide? So, I think there are lots of problems. Someone has to elaborate and think about a more rigorous approach and economic theory to provide a good dialogue on this.”*

7.9. Hypothecated tax

The hypothecated tax approach in the form of indirect taxation that is imposed by the authorities to end-users (patients). It can be described as the process of allocating tax revenues to a specific end, or- in certain cases- ensuring that they are not spent on one particular end. An additional fee (tax) would be added to the regular medicine price for a patient. Then, the collected revenue would be divided and distributed via governmental institutions to medicines manufacturers as a form of supportive financial subsidy. Subsidies' role is to neutralise increased operational costs that medicines suppliers have to cover on their own.⁷⁷

In the UK, some new tax increases were purposed linked with spending commitments, even though hypothecation has never been the preferable taxation option. Hypothecated taxation was introduced in the UK to a couple of public sectors. The model example of a hypothecated tax in the UK tax system is National Insurance Contributions (NICs), the notable amount of which is automatically spent on social security benefits.

An example of hypothecated “tax”/ (fund) model implementation in the pharmaceutical sector is from Australia. The Life-Saving Drug Program (LSDP) is a hypothecated fund that's main objective is to cover fully the price of life-saving medicines and agents used to treat rare conditions that have been rejected by HTA due to not producing satisfactory cost-effective results, despite being clinically effective. Without the governmental subsidy, very few Australian citizens would be able to afford therapy due to financial burdens (hundreds of thousands of Australian dollars). A panel of experts with the former Deputy Chief Medical

Officer are responsible for the evaluation of medicines for funding and for advising the Chief Medical Officer.⁸³ The government subsidised initiative used in Australia to provide alternative access to medicines (life-saving and used to treat rare diseases) is referred to as “Needs” Based Funding. Like in a classic hypothecated “tax”/ fund model the collected funds (in 2017/2018 the government invested \$128 million) are relocated to medicines manufacturers in exchange for access to medicines.

Table 13. Hypothecated Tax model

HYPOTHECATED TAX in the generics sector SUSTAINABILITY FEE	
Description	Additional payment is added to the retail price (for patients) per box of Rx and OTC medicines and dietary supplements dispensed at a retail environment, independently of reimbursed amount. Revenue is collected to a separate fund with the purpose to be transferred to manufacturers of medicines at-risk proportionally to their volume of sales
Aim	To cover the increased operational cost that medicines suppliers have to cover on their own, to secure medicines supply
Direct point of impact	Taxes / Subsidies
Potential for targeted use	Collection stage: No (permanent fee applied to a group of medicines/products, not applicable directly to medicines at-risk) Redistribution stage: High (to manufacturers of medicines at-risk)
Impacted stakeholders	Manufacturers of at-risk medicines (+), patients (-/+) (patient fee), on-patent, OTC and dietary supplements manufacturers (-)
Entrance incentives	No
Exit prevention / Retention incentives	High
Mechanism of action	Indirect taxation, end-user fee
Possible concerns	Criteria to redistribute funds, establishing sustainability fee amount, Impact of inflation, cost of collection/redistribution, patients' willingness to pay and accept the regulation, relation of collected funds to real needs to ensure the effect, tangible effects which can be associated with the sustainability fee

All pricing models for generics that require additional patients' co-payment (hypothecated tax, cost allocation or cost-plus model) have uniformly been appraised by experts as having a very low implementation potential. There may be some European countries (Denmark, Sweden or Norway) that due to their long-standing tradition of collective responsibility and common, public good, could possibly consider the implementation of a pricing policy model that requires an additional end-user (patient) fee. However, in the vast majority of European countries, the strong objection of decision-makers and patients is expected as there is no social acceptance of extra payments, even the symbolic ones. Additionally, the financial burden associated with a medication purchase stands in opposition to the idea of social justice and can contribute to deepening social inequalities related to access to affordable healthcare.

- *"All these payments and co-payments for drugs brought a tremendous financial burden"*

- *“Hypothecated tax is probably applicable in Denmark or Sweden or Norway. In Central and Eastern Europe, we hate the concept of collective property.”*
- *“You will not be able to convince politicians and decision-makers that they have to announce on television that from tomorrow onwards, all patients will need to pay an additional co-payment because we consider healthcare to be a public good. And they would argue look, we already pay through our taxes for healthcare and there is just no rationale for increasing prices.”*
- *“Increased prices create some sort of increasing health inequalities and we have measured and analysed health inequalities in access to medicines. They increased with out-of-pocket payments and then we have carried out also some analysis on the relating the out-of-pocket payments with the catastrophic effects.”*

7.10.Value-based pricing (VBP) for generic medicines

A value-based pricing (VBP) concept exists and is well known for innovative medicines. The main aim of the value-based approach is to assess if the medicine provides the benefits valued by a society which justify its cost. Health technology assessment (HTA) is a widely used tool in informing decisions on the approval and pricing of medicines. Different approaches to calculating the drug’s value to society might result in a realistic value being agreed upon, thus ensuring better access to medicines. VBP aims to assess wider-based aspects of societal value, and the drug company may be asked to justify its claim about the value of its product. A basic cost-effectiveness price will apply unless one of three categories is met for higher thresholds: (1) greater burden of illness — the severity of the condition and the level of unmet need, (2) therapeutic innovation — novel agents for new treatment targets and potentially revolutionary disease treatments will attract higher thresholds for pricing, (3) wider societal benefit — economic well-being of the population as well as direct healthcare costs.⁸⁷

Value-based pricing for generics is a newly proposed concept. It is anticipated that forced price erosion of off-patent and generic medicines may lead to buying a wealth of valuable benefits at the fraction of the cost of innovative patented medicines. Simply showcasing how cheaply and cost-effectively the treatment benefit is bought with generic medicines would at least limit the continuing price pressures.

It is argued that current prices of generic medicines do not reflect their value, which means these medicines are greatly undervalued.

- *“Generic industry is the victim of its own message that generics are about saving costs. They should shift towards focusing on cost-effectiveness of generics.”*
- *“Healthcare payers and HTA agencies should reassess the value of a medicine once it becomes off-patent because, in my opinion, and some of these medicines have been on the market for a very long time. The price has decreased, but they are actually very valuable medicines, even more, valuable than some more expensive innovative therapies. I would suspect that if we look at the cost-effectiveness of generic medicine, which has a much lower price and maybe generates similar effectiveness and compares them to these innovative medicines, then we are actually as a society better off with using these variable old generic medicines”.*
- *“In a market environment the price only goes down, this does not reflect the fact that these are old but very valuable medicines. You mentioned cost-plus pricing of generic medicines [guaranteed margins/ fees] why not look at value-based pricing of generic medicines?”*

- *“What is the value of these medicines, especially at the lower price of the generic version as compared to maybe the most innovative treatment which is hugely expensive but usually offers limited additional clinical benefit? And we know that physicians have a tendency to switch directly to these new expensive medicines. So, then you have to say to your politician or decision-maker, look, we see that there are shifts and prescribing practices through these new medicines that only offer a limited health gain, but cost a lot of money. Your better strategy would be that you increase the price of the generic medicines a little bit. Increasing the price of a generic medicine a politician will not understand, because it’s completely irrational, but you have to explain it within the context of the market entry of these new innovative treatments. And so, I would also be in favour of having a look at the value-based pricing approach towards the generic medicines”.*

It seems reasonable not only to focus on single molecule but consider the whole therapeutic class (both originators and generics) while performing the value assessment. Generics should not be perceived only as medicines with cost-saving potential but also as agents that represent health benefits that can be measured.

- *“I think you have to look at the certain therapeutic domain where you see that over time there are different classes of medicines that treat those diseases. Maybe for one of the earlier classes, the patterns have expired. You have these cheaper generics available and then a new product class of innovative treatments comes on to the market and usually they offer an incremental health benefit but at a hugely expensive price”.*
- *“We should reassess the value of medicines and compare the cost-effectiveness of a generic medicine with that of those innovative medicines that come onto the market”.*

Implementation of value-based pricing seems to be challenging due to limited feasibility and not straightforward applicability to the generic medicines sector. So far VBP was introduced to sectors with no or minimal competition. In some European countries, VBP or HTA have not been implemented yet with some forms of substitute scoring systems used.

- *“If we want something feasible that could be implemented in the next two or three years, let’s not go to value-based pricing. If we are optimistic though, I say yes, of course. I mean we should aim for value-based pricing. We want to prioritise something more feasible, maybe value-based pricing. I’m not saying it’s not a good thing, but I’m saying that for most of the generic it’s more about price competition”.*
- *“For new drugs, it is difficult to produce studies about the clinical effectiveness and cost-effectiveness. All the discussion about thresholds of cost-effectiveness, what does it mean exactly for value-based pricing. So, I think that we have so many problems at the moment, that I wouldn’t be in favour of extending these problems to other drugs (generics). Value-based pricing in my view exists because there is no competition because we have a new [medicine] that is on patent, they have the monopoly and exclusivity, there is no competition, and the regulator needs a way to pay a price that is acceptable for the society. However, I’m strongly in favour that new drugs are re-evaluated from time to time. To the evolution of the market, to the entry of other drugs that may have similarity, therapeutic effects and so on”.*
- *“In terms of feasibility, I sense the problem. The HTA departments or agencies in different countries have different levels of development. What we’re using in Romania, for example, is not necessarily a core HTA, it’s a scorecard. That it’s easy to be used, but it’s not actually reflecting the value”.*

7.11. Volume for savings

The volume for savings model (sometimes referred to as gain sharing approach) is an attempt to counteract blind linear price cuts of generic medicines that happen in several European countries in order to limit pharmaceutical expenditures. Instead of blind price reduction, it is proposed that generic drugs will lower their prices in the following year to provide savings by means of linear price decreases for the volume increase in the current year.

The volume for savings approach is considered to be a safe option for the governments which are looking for savings and at the same time a tool that helps generics producers to increase their volume sales. However, the price reduction would be applied to generic medicines at the moment of achieving an increase in volume share.⁸⁸

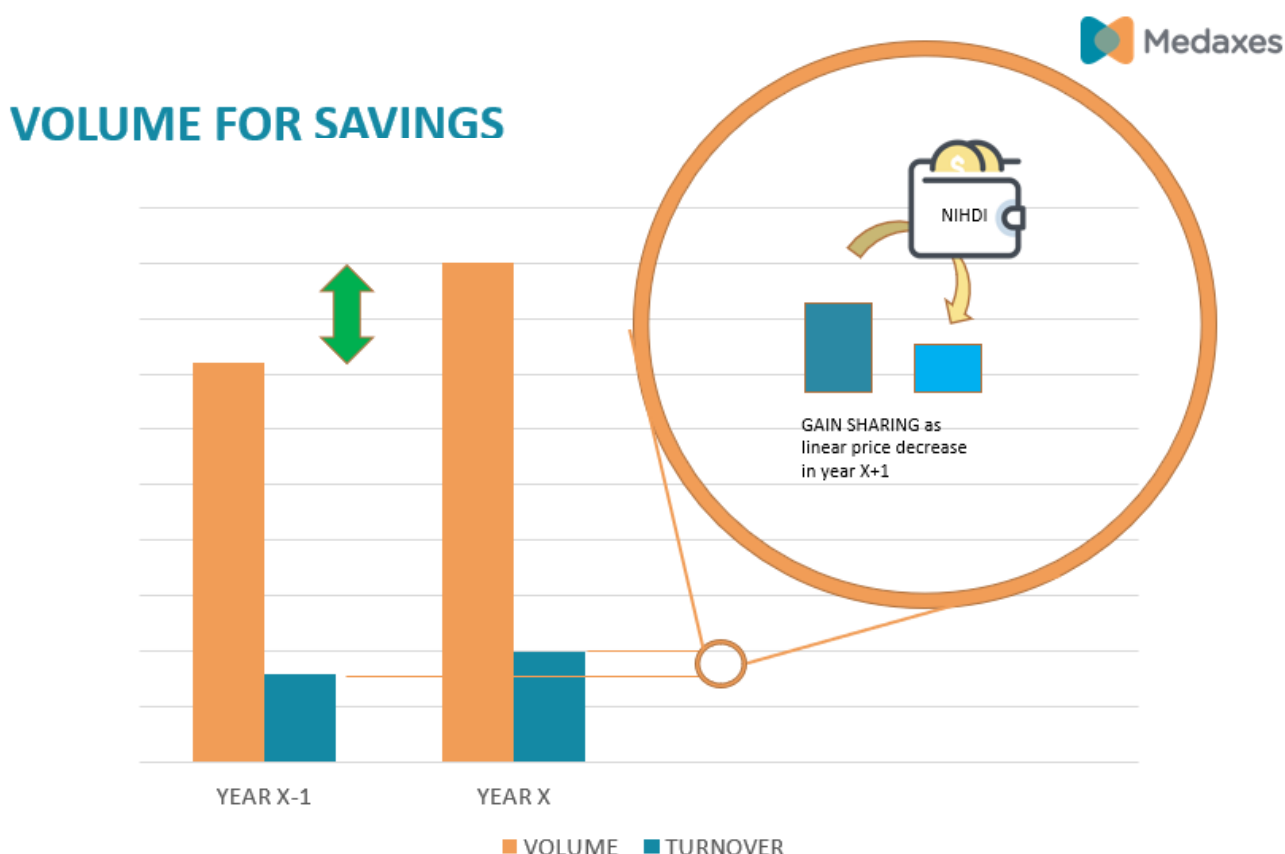
Volume for savings opportunities:

- The condition that the volume must increase in the preceding year for the linear price cut to be applied
- Incentivise governments to undertake measures leading to increased generics uptake (if the volume is not growing it means there is no room for price cuts and further savings)

Volume for savings risks:

- For individual companies, part of the growth is “clawed back”
- Applicability is limited to European countries with mandatory blind price cuts (e.g., Belgium)

Scheme 4. Demonstration picture – by courtesy of Medaxes⁸⁸



If the volume share of generics increases in year X compared to year X-1, generic manufacturers will give back part (a certain percentage) of the resulting increased turnover by means of linear price decreases in the year X+1.

Experts emphasised that the primary aim is to enhance healthy competitiveness for generic medicines. The generic sector is the business of volume but cutting prices according to achieved volume is not necessarily a measure that boosts competitiveness.

- *“When competition is very low, then the price is higher when competition is high then we may lower the price. I think this is what we expect to have- high competition. The higher volume of generics, even if in the end this is what will happen, what we want is to enhance competition. I don't see by cutting the prices according to the condition that you achieved a higher volume”.*

The specificity of the national pharmaceutical market may determine if the generic market share is going to increase, regardless of introduced new pricing regulations.

- *“Actually, that is related to a product price reduction to whether they would lead to a greater market share. In Greece, for instance, generics represent a very small market share, which is about 30%. And despite the overall policies implemented, this market share has not been increased at all”.*
- *“We need to take into account the generic market share in every country because there is something different if it's 30% or if it's 70% when we talk about volumes. The volume situation is also different in therapeutic areas or groups”.*

The “volume for savings” so as “price heaven for essential medicines” concept was proposed in Belgium as the consequence of the introduction of austerity measures to the pharmaceutical sector seeking savings.

7.12. Price heaven

Initially, the idea of a “price heaven” was proposed for “essential medicines” in Belgium during the Covid-19 global pandemic. Medicines listed as essential medicines in Belgium are not subjects of price cuts imposed by austerity measures for pharmaceutical specialities. The price decrease that has already been applied for essential medicines is cancelled due to the justified threat of their withdrawal from the Belgian market caused by significant price erosion. The price heaven is the response to excessive price cuts that may lead to essential medicines shortages and unmet supply needs.⁹³

Generic medicines being affordable therapeutic options should be also protected from unjustified price reductions that in most cases may result in generic market concentration and increased risk of supply disruption.

7.13. Key takeaways

- There are three new pricing policy models – tiered pricing, de-linkage from originator price, and automatic indexation that represent visibly higher implementation potential than the other proposed models.
- The tiered pricing model addresses simultaneously two aspects critical for the generic market in Europe – it is adjustable to the competitiveness level and promotes sustainability. Moreover, the tiered pricing model has a broad applicability spectrum and potentially can be introduced in countries with reference pricing so as countries with free pricing schemes for generic medicines.
- The tiered pricing model responds to changing competition levels on the market by either decreasing the required price with new market entrants or increasing in the opposite situation
- The de-linkage from originator price either partial or complete variant of this model is focusing on eliminating the originator's reference price impact on generic medicines prices. Breaking the price linkage would help to eliminate restraints that impede the development of a sustainable and competitive generic market in Europe.
- The de-linkage from the originator price model should be applied cautiously either when a certain market is mature or when predicted to have multiple competitors due to high market volume, with the main benefit to prevent the originator from forcing generic competitors' prices to economically nonviable levels.
- The automatic indexation models aim to compensate for higher costs due to inflation or rising regulatory burden by automatically adjusting prices based on a given index value; their acceptability largely depends on how much risk associated with inflation a public payer is ready to accept to prevent market withdrawals.
- Other pricing models for generic medicines that have been evaluated and considered less feasible and less effective are: tax credits, guaranteed margins, One-in-one-out (OIOO/OIXO), value based pricing for generics, volume for savings and price heaven.
- New pricing models involving additional end-user (patient) fees (hypothecated tax, cost allocation) are uniformly considered as having a very low implementation potential due to very low social acceptability with just a few exceptions (Denmark, Sweden, Norway) with a long-standing tradition of collective responsibility and the public good.

8. Strategic recommendations for implementation of policy models to ensure healthy competitiveness and economic viability

Strategic recommendations are summarized in the points below:

1. Recommended activities for country decision-makers in regard to competition-sensitive approach.
 - a) Revise existing policies whether they enable actions towards improving competitiveness.
 - b) If existing policies are insufficient to improve competitiveness, implement new or adjust existing pricing models taking into account your country archetype.
 - c) Monitor and analyze competitiveness level in reference groups based on sales data.
 - d) React to deteriorating competitiveness level.
2. When considering policy changes relating to generic medicines, apply holistic approach considering both general and market specific aspects.
3. A proper balance has to be achieved and maintained between generating savings for the system and revenue for manufacturers with the ultimate goal to ensure access to affordable medicines for patients within the available budget.

The most fundamental recommendation for decision and policymakers would be to start consistently monitoring the level of competition in reference groups (using the Herfindahl-Hirschmann Index), notice the changes in a negative direction and take action when deterioration of competition is considered a threat to continued supply instead of waiting inactively until medicines are no longer supplied.

To implement such competition-sensitive pricing policies, one has to rely on sales data and their repeated analysis. The administrative burden associated with market data analysis is an absolutely necessary investment in healthy competitiveness and sustainability of supplies.

Healthy competitiveness requires a proper balance between generating savings for the system and revenue for manufacturers with the ultimate goal to ensure access to affordable, up-to-date medicines for patients within the available budget.

When monitoring the competition level, one has to differentiate between molecule suppliers and medicine manufacturers – numerous manufacturers who rely on the same single source of a molecule translate into a low level of competition.

Most often in current policies in European countries, the objective is to generate savings regardless of the impact on competition. If savings are imposed too aggressively, it is certain to backfire in a form of medicines shortages. For example, in the case of austerity measures assuming blind repetitive price cuts with a competition-sensitive approach you would monitor the competition level and put on hold further price-cuts in a certain reference group when the competition level significantly worsens in repeated measurements. Usually, the first affected parties would be smaller competitors. The reason for stopping

the price cuts would be that you may be getting close to the point beyond which price levels are unsustainable.

A recommended pricing policy system should offer tools to be used if competition weakens.

When you identify a situation that warrants measures to prevent further deterioration of competition consider your existing classic pricing policies and whether variants applicable to strengthen competition are achievable in the current legal framework. If yes, then use these variants. If not, you need to make legal adjustments to existing policies to make them more flexible. In both cases, you are encouraged to consider introducing new policy models discussed in the report.

While discussing implementation strategy for new generic policy models in a certain country, a holistic approach has been advocated to consider both general issues (restrictiveness of existing medicines pricing policies, healthcare system features, impact on innovative products, flexibility in allocating funds for healthcare, social acceptance, attitudes towards generic medicines) and market-specific (market characteristics: high/low volume, number of suppliers of molecules, number of manufacturers, their volume market shares).

The tiered pricing model is universally ranked on top, both in terms of effectiveness and feasibility across all country archetypes (A2-A5), with archetype A2 countries scoring highest and A4 – the lowest. Countries representing archetypes A3 and A5 have similar positive views on the application of tiered pricing to their systems.

From a long-term perspective, a tiered pricing model is seen as a sustainable solution ensuring competitiveness and strengthening economic viability, however, it requires market monitoring to collect data using appropriate supportive IT infrastructure. This model could work both in regulated and free pricing countries. Setting up tiers which are far apart will drive prices down with relatively few competitors however for some molecule markets such a steep price decrease may introduce market withdrawals and return to the higher tier.

In the original Canadian Tiered Pricing Framework, the reference price of the originator is established once at the moment of the first generic entrant and will be used for all subsequent assessments regardless of later fluctuations of the originator's price. This solution resembles another model assessed in the report, partial de-linkage from the originator price.

De-linkage from the originator price is ranked second high for both effectiveness and feasibility for country archetypes A3 and A5 (Portugal and Romania, respectively).

For countries representing archetypes A2 (Belgium) and A4 (Spain), this model is considered less effective and feasible compared to the countries mentioned above. It may be inferred that de-linkage from the originator price is most valued and accepted in countries with a high percentage forced decrease of the first generic price as referenced to the originator, especially if combined with high clawback/payback.

For countries within A2 (Belgium) and A3 (Portugal) archetypes with less restrictive existing policies, higher marks are consistently given to the guaranteed margins/fee model than for countries from archetypes A4 and A5. Besides controversies about transparency and credibility of cost data, the model could involve

setting different tiers for margins related to the number of competitors. Any cost-plus model removes incentives for cost optimisation which makes these models rather unsustainable in the long-term despite short-term economic viability boost.

The next best model is Value-Based Pricing for Generics: it is ranked as extremely effective for countries A5 (Romania) and mid-values for archetypes A2-A4 whereas it is ranked mid- to low- for feasibility for all archetypes. Similarly, to the One-In-One-Out model, Value-Based Pricing for Generics is perceived more as a strategic mindset changer by switching the narrative from “generics provide savings” to “generics provide treatment benefits at exceptionally affordable cost” much lower than current innovative treatments. The biggest challenge universally would be to perform value-based assessments in countries with limited HTA capacity and extensively for whole therapeutic classes/indications including all available treatment options.

The One-In-One-Out approach for generics was collectively classified as low effectiveness and low feasibility level across all country archetypes. It is more a strategic approach to communicate that before considering any new regulatory burden on generic manufacturers, legislators have to note the worsening imbalance between growing costs and decreasing revenues due to restrictive price policies. In this sense, it is more applicable in countries with highly regulated markets and restrictive price policies (A3-A5).

The tax credits model has been uniformly assessed as having very low feasibility and mid- to low-effectiveness with A2 archetype (Belgium) potentially mid-effectiveness provided it is applied to all off-patent and generic medicines to create a level playing field.

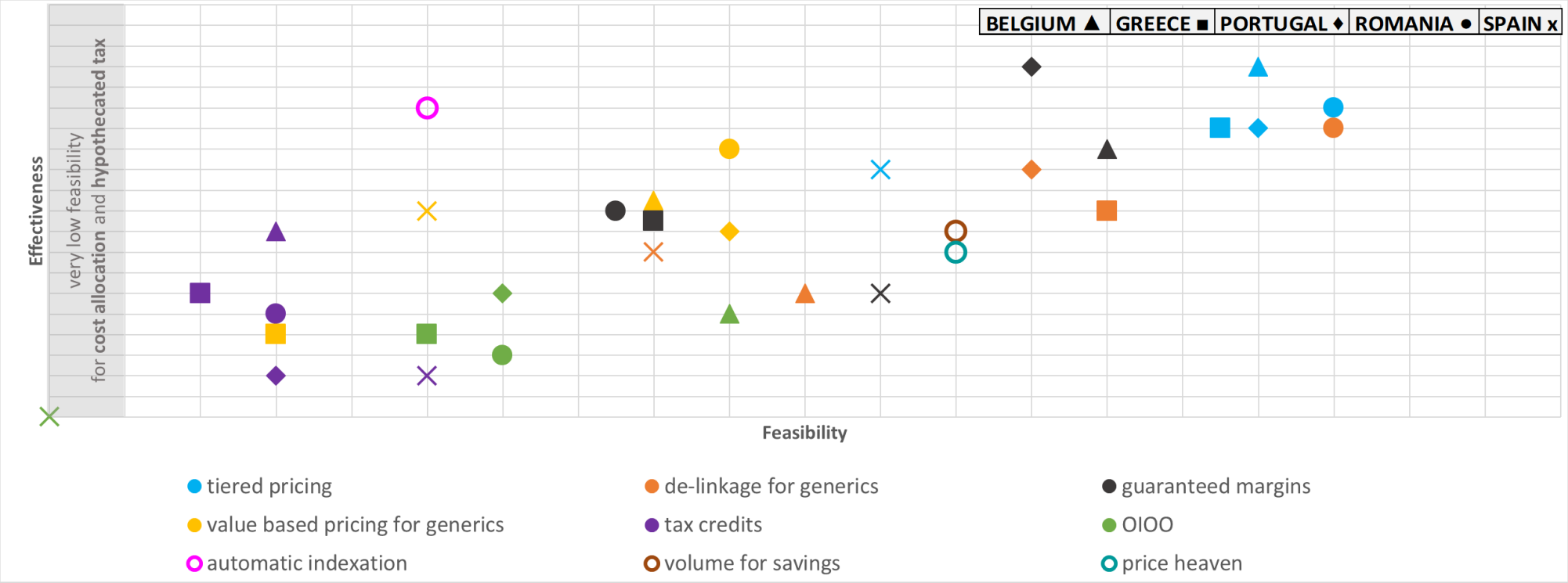
The remaining three models have been assessed internally and their relative position on the diagram reflects this internal assessment.

Volume for savings and price heaven have been proposed in archetype 2 countries where systematic price cuts are in place (Belgium). It appears that volume for savings would be relatively effective and feasible however in practice achieving volume increases might be a challenge. Price heaven has both effectiveness and feasibility measures similar to volume for savings and appears to be a temporary tool to address medicines needs during the COVID-19 pandemic.

Automatic indexation is assessed as highly effective but with low feasibility. The more budgetary means are available, the more acceptable automatic indexation would be (e.g., Germany). The main concern for feasibility would be to what extent to share the risk of inflation between the payer and medicines manufacturers. It may be claimed that such model should be considered as a transient measure to address the economic cycles with higher inflation levels

New pricing models involving additional end-user (patient) fees (hypothecated tax, cost allocation) are uniformly considered as having a very low implementation potential due to very low social acceptability with just a few exceptions (Denmark, Sweden, Norway) with a long-standing tradition of collective responsibility and public good.

Figure 11. Models pairwise comparison results



9. Methodology

9.1. Rx market in European countries

Table 14. Generic products definitions (IQVIA)²²

Classification	Protection	Pre/post protection expiry	Name type	Launch status
Generic products	Never protected	Post protection	-	Subsequent launch
<ul style="list-style-type: none"> Never protected, post protection expiry, subsequent launch products carry the standard generic product description. These products are launched after the protection of the original product had expired, into a market without exclusive manufacturing or marketing rights, and therefore without protection themselves. This category accounts for ~98% of the total IQVIA classified generic market 				

Classification	Protection	Pre/post protection expiry	Name type	Launch status
Generic products	No longer protected	-	INN unbranded	-
	No longer protected	-	Company branded	-
<ul style="list-style-type: none"> No longer protected, INN unbranded or company branded products are generic products which were launched onto the market prior to the expiration of the protection on the original product These authorised early entry products are classified as generics once the protection on the original product has expired, and free generic competition is allowed. This category accounts for ~2% of the total IQVIA classified generic market 				

Table 15. Non-generic products definitions (IQVIA)²²

Classification	Protection	Pre/post protection expiry	Name type	Launch status
Non-Generic products	Protected	-	-	-
<ul style="list-style-type: none"> Any product which is protected against generic competition is classified as non-generic product 				
Classification	Protection	Pre/post protection expiry	Name type	Launch status
Non-Generic products	No longer protected	-	Branded	-
<ul style="list-style-type: none"> No longer protected, branded products are original brands which once had the benefit of protection, which has now expired Brands in this category face legal generic competition. 				
Classification	Protection	Pre/post protection expiry	Name type	Launch status
Non-Generic products	Never protected	Post-protection	-	First launch
<ul style="list-style-type: none"> Never protected, post protection expiry, first launch products are the first appearance of the active ingredient in any form, for which exclusivity was never granted on the product. Such products are viewed as being launched post-protection expiry. Because they are first launch products, they set the market for that active ingredient and are classified as non-generic These products account for ~8% of the total non-generic market. 				

Data received from MFE²² (IQVIA database) were used to prepare charts presenting the Rx market in European countries in the years 2016-2021. In Table 14 and Table 15 definitions of generic and non-generic products used in this data are presented.

The charts present data for individual countries and years. The countries are sorted starting with the country with the lowest value of standard units (one standard unit equals one tablet/syringe) in 2021. The charts show the number of standard units of generic and non-generic medicines in particular years and the percentage share of generic drugs in the entire drug market in the analysed period. Biosimilars are excluded from the analysis.

9.2. Models pairwise comparison

Pairwise comparison is a process of comparing candidates in pairs to judge which of each candidate is preferred overall. Each candidate is matched head-to-head (one-on-one) with each of the other candidates.

All experts were asked to compare pairs of six new pricing models for generic medicines (tiered pricing, de-linkage for generics, guaranteed margins, value-based pricing for generics, tax credits and OIOO) on two dimensions: effectiveness and feasibility. The two new pricing policies (hypothecated tax and cost allocation) have uniformly been assessed as having very low feasibility and they were not included in the comparison. To make an assessment, five categories of answers were given in each dimension and each category had an assigned point value, as presented below.

Effectiveness	Feasibility	Points
is much more effective than	is much more feasible than	4
is more effective than	is more feasible than	3
is as effective as	is as feasible as	2
is less effective than	is less feasible than	1
is much less effective than	is much less feasible than	0

The results for the model were then summed up in rows, and the obtained values were the coordinates on the x-axis (feasibility) and the y-axis (effectiveness). The model was not evaluated against itself. The result for an inverse comparison was the reciprocal of the score, e.g., if tiered pricing vs guaranteed margins: 3 points, then guaranteed margins vs tiered pricing: 1 point.

All comparisons and calculations were performed in an MS Excel file.

Results of this pairwise comparison were presented on the implementation matrix – scatter plot chart, where each model had a different colour, and each country had a different mark.

9.3. Systematic Literature Review

The objective of this systematic literature review (SLR) was to:

- Update the comprehensive literature review on the “Impact of European pharmaceutical price regulation on generic price competition: a review.” (Puig-Junoy *Pharmacoeconomics*. 2010;28(8):649)
- Identify payer archetypes and additional national case studies evaluating the impact of the current price regulations on the generics market and available literature on new pricing models for generics in Europe.

The methodology of this SLR was followed in line with NICE and CRD guidelines and it was organised according to the following phases:

- Search strategy: search strategy was developed and implemented in selected bibliographical databases
- Selection of articles: abstracts and full-text screening according to inclusion and exclusion criteria on the basis of the research question
- Data extraction & quality control: extraction and quality control of data from the included articles
- Data synthesis: summary of findings.

The methodology associated with the search strategy, studies selection, and data extraction is provided in the following sections.

9.3.1. Bibliographical database

After having defined the search keywords as well as inclusion and exclusion criteria, the search was performed in the following databases:

- Medline via Ovid
- Embase via Ovid
- The Cochrane Library
- The University of York Centre for Reviews and Dissemination
- EconBiz.

9.3.2. Search strategy

The search strategy was prepared based on Puig-Junoy’s 2010 original search methodology. All used keywords were: “reference price” and “pharmaceutical”; “reference pricing” and “pharmaceutical”; “generic”, “pharmaceutical” and “reimbursement”; “generic”, “pharmaceutical” and “price competition”; “generic”, “pharmaceutical” and “discount”; and “generic”, “pharmaceutical” and “rebate”.

9.3.3. Selection process

Inclusion and exclusion criteria are reported in Table 16.

The review was focused on studies conducted in the following geographical areas: Europe.

Only articles in English and Spanish were included.

A timeframe restriction of the year 2009 onwards was applied as it was an update of the existing SLR.

Table 16 Inclusion criteria (PICOS)

PICOS	Inclusion
<u>P</u> opulation	No restrictions
<u>I</u> ntervention	Price capping and/or regulation of the reimbursement rate (reference pricing or similar systems)
<u>C</u> omparators	Not defined
<u>O</u> utcomes	<ul style="list-style-type: none">Studies had to present empirical results of a quantitative nature for EU countries on the impact of price capping and/or regulation of the reimbursement rate (reference pricing or similar systems) on price dynamics, corresponding to pharmacy sales, in the generic drug market. Studies that will provide country specificities will be captured to start building on payer archetypes.The studies included were required to contain as one of their outcome variables, relative either to generics or to branded and generic pharmaceuticals together:<ul style="list-style-type: none">The price* paid by the final consumer to the pharmacy (with or without taxes)The price* paid by the pharmacy to the wholesalerThe price* paid by the wholesale distributor to the manufacture <p>The discount received by pharmacies on their purchases from distributors and manufacturers on top of the official reimbursement rate</p>
<u>S</u> tudy design	Comments, editorials and letters to the editor or director were excluded.

First, references were imported into an Endnote database and after eliminating duplicated articles, they were imported and saved as an excel file. The list of titles and abstracts and full-texts were screened by two independent reviewers according to the defined inclusion and exclusion criteria, in order to select relevant articles pertaining to the topic of interest. Discrepancies were resolved by a consensus or by a third reviewer. All references and analysts' decisions were saved as an Excel file called the inventory file.

References were classified into one of two categories:

- Included
- Excluded.

The first category included articles that appeared relevant at the first screening and moved to full-text screening to confirm their inclusion. The second category included references for which it is obvious from the title and abstract that they should be excluded. The primary reason for exclusion was recorded. Potential reasons for exclusion were:

- Not relevant population
- Not relevant intervention
- Not relevant comparator
- Not relevant outcome
- Not relevant study design
- Duplicate.

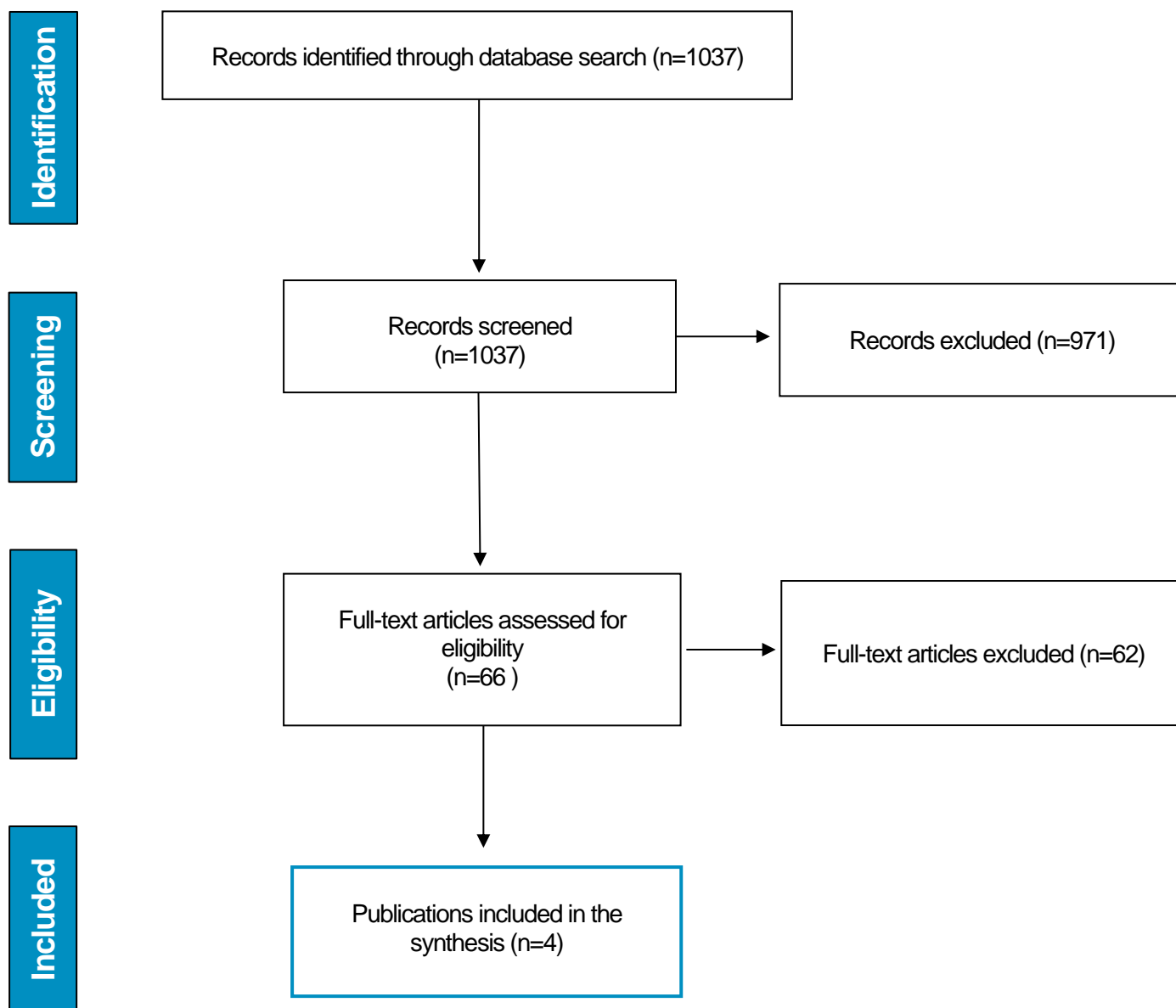
9.3.4. Data extraction process

Data from studies included in the review were extracted during the reports writing process.

9.3.5. Results of the literature search

Overall, 1,037 hits were identified in the selected databases. After title and abstracts screening, 971 records were excluded (Figure 12). 66 references proceeded to the full-text review phase and 62 publications were excluded after that stage. Finally, data from 4 studies were extracted.

Figure 12. PRISMA chart for SLR



9.4. Targeted Literature Review

The objective of this targeted literature review (TLR) was to identify payer archetypes and additional national case studies evaluating the impact of current price regulations on the generics market and available literature on new pricing models for generics in Europe.

The review was organised according to the following phases:

- **Search strategy:** search strategy was developed and implemented in selected sources
- **Selection of articles:** abstracts and full-text screening according to inclusion and exclusion criteria on the basis of the research question
- **Data extraction:** extraction of data from included articles
- **Data synthesis:** summary of findings.

The methodology associated with the search strategy, studies selection, and data extraction is provided in the following sections.

9.4.1. Sources

First, a supplementary search in Medline & Embase via Ovid databases was conducted to find publications that answered key questions and were not covered by the SLR search strategy.

Then, other sources with potentially relevant information were identified. These sources were divided into six groups:

1. International sources
2. Country specific sources
3. Databases
4. Sector specific journals
5. News feed
6. Reports

9.4.2. Search strategy

In each of the sources searched dedicated search strategy was used, focused on the goal of identifying all potentially relevant materials for the project.

9.4.3. Selection process

All identified potentially relevant materials were verified according to key questions, defined for the purpose of this report. Additional criteria were geographical scope (mostly Europe, but good practice examples from other regions were also included) and up-to-date data presented.

9.4.4. Data extraction process

Data from studies included in the review were extracted during the reports writing process.

10. Abbreviations

Abbreviation	Definition
AMP	Average Manufacturer Price
ATC	Anatomical Therapeutic Chemical Classification
CPI	Consumer Price Index
DDD	Defined Daily Dose
ERP	External Reference Pricing
EU	European Union
EUR	Euro
GDP	Gross Domestic Product
HHI	Herfindahl-Hirschman Index
HTA	Health Technology Assessment
INN	International Non-Proprietary Name
IRP	Internal Reference Pricing
LSDP	Life Saving Drug Program
MAH	Marketing Authorization Holder
MFE	Medicines For Europe
mn	Million
NHS	National Health System
NICs	National Insurance Contributions
OECD	Organisation for Economic Cooperation and Development
OIOO	One-In-One-Out
OIXO	One-In-X-Out
pCPA	Pan-Canadian Pharmaceutical Alliance
PPI	Producer Price Index
PPIs	Proton Pump Inhibitors
R&D	Research And Development
Rx	Prescription Medicine

Abbreviation	Definition
SLR	Systematic Literature Review
TPF	Tiered Pricing Framework
UK	United Kingdom
US	United States
VBP	Value-based Pricing
WHO	World Health Organization

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13. Appendix

13.1. Classic pricing tools

Table 17. External reference pricing

1. Impacted parameter		2. Basket of countries		3. Basket of products	
1.1 final price (ex-factory price, pharmacy purchasing price, pharmacy retail price)	many European countries	2.1 # countries in the basket	The basket of the reference countries is calculated individually for each country. Some countries have specific restrictions regarding the number of countries in the basket. Additionally, some of the European countries require to have in the basket at least 50% of the countries with an already established price of reference product – this requirement simplifies the process.	3.1 only reimbursed in the ref. country	majority of European countries
1.2 reimbursement amount (reimbursement price)	Germany (since 2011)	2.1.1 (3-4) countries	France, Portugal, Croatia, Cyprus	3.2 regardless of reimbursement status	Austria, Portugal
1.3 reimbursement rate	some of European countries	2.1.2 (7-12) countries	Denmark, Romania	3.3 active substance	Poland, Italy, Spain, France, Germany, Portugal, Hungary
		2.1.3 (>20) countries	Austria, Italy, Poland	3.4 therapeutic class	Poland, Germany, Hungary, Czech Republic
		2.2 only Eurozone countries as ref.	majority of UE countries	3.5 pharmacological class	Bulgaria, Germany, Hungary, Czech Republic, the Netherlands
		2.3 Eurozone + European Economic Area (EEA)	Hungary, Poland		
		2.3 Eurozone + non-Eurozone countries	Switzerland		
		2.4 Method of countries selection	Great variability among countries		
		2.4.1 GDP (per capita)	based of comparable GDP		
		2.4. 1.1 Influence of GDP - examples	Changes in the mix of basket countries leads to price changes. 1) Croatian removed in 2012 France from its reference basket and replaced by the Czech Republic. EFFECT – reduction in most pharmaceutical prices. (Czech Republic GDP < France GDP). 2) Spain – prices increased when countries with higher GDP per capita than Spain were included in the Spanish reference basket. 3) Slovakia – where ERP initially tended to result in higher prices relative to neighbouring countries with similar income levels due to reference country selection, particularly because Germany and originator country prices were used to calculate reference prices.		

2.4.2 market size	market size and socioeconomic condition
2.4.3 other	countries' individual methods of composing reference basket

4. Setting the ref. product		5. Function of ERP		6. Algorithm for parameter calculation		7. Price re-evaluation (after the initial price is set)	
4.1 based on the cheapest medicine	Poland, Spain, Bulgaria, the Czech Republic	5.1 ERP main criterion for price setting	France, Portugal, the Netherlands (majority of European countries)	6.1 based on avg. price of medicines	Croatia, Hungary	7.1 annual re-evaluation	Norway (re-evaluation of the max. price of 250 active ingredients with the highest turnover)
				6.1.1 based on avg. the 3 or 4 lowest prices	Greece, Norway, Slovakia, Czech Republic	7.2 as needed due to currency adjustment	Ireland (2012- currency-adjusted ex-factory price of the drug in ref. countries)
4.2 percentage of orig. price	some European countries	5.2 ERP as a supportive criterion for price-setting (informative role)	Poland, Italy, Spain	6.2 the lowest-priced medicines	Bulgaria, Hungary, Italy, Poland, Spain	7.3 twice a year	Slovenia
4.3 if there is no ref. price available in ref. countries - the alternative countries can be used as reference	Bulgaria, Croatia, Cyprus	5.3 ERP used only once at launch	Hungary	6.3 the lowest-priced generic medicines	Bulgaria, France, Latvia	7.4 frequent	Greece, Latvia, Lithuania and Slovakia
				6.4 based on the percentage of originator medicine price	some European countries	7.5 no or less frequent	Austria, Cyprus, Denmark, Estonia, Germany, Hungary, Iceland, Luxembourg, Poland
				6.5 based on the weighted average of all products in one group and calculated by regression analysis (econometric model)	Germany	7.6 by using public official price databases to compare prices at ex-factory level	majority of the EU countries
				6.6 based on the weighted average price of medicines	The Netherlands		
				6.7 price "similar" to ref. countries	France		

Table 18. Internal reference pricing

1. Impacted parameter		2. Comparability criteria		3. Algorithm for calculating the parameter		4. Frequency of update	
1.1 Price	No direct impact	2.1 ATC-5 (active ingredients)	Belgium, Bulgaria, Denmark, Estonia, France, Ireland, Lithuania, Romania, Slovenia, Poland, Finland, Italy, the Netherlands, Portugal, Spain, Turkey	3.1 The lowest price		4.1 Every two weeks	Denmark
1.2 Reimbursement limit (amount)	Germany, many European countries	2.2 ATC-4 (chemical subgroup)	The Netherlands	3.2 Average price	The Netherlands, Greece, Hungary, Romania	4.2 Monthly	Italy
1.3 Reimbursement rate	some European countries	2.3 ATC-5 and ATC-4	Bulgaria, the Czech Republic, Hungary, Slovakia, Greece	3.3 Average of the lowest 3 prices	Spain	4.3 Quarterly	Estonia, Portugal, Slovakia, Belgium
		2.4 ATC-5, ATC-4 and ATC-3	Germany, Italy, Latvia, Poland	3.4 Average of the lowest 5 prices	Portugal	4.4 Every 6 months	The Czech Republic, Slovenia
		2.5 ATC-5 and ATC-3	Czech Republic, Hungary, Romania, Slovakia	3.5 Combination of prices	Germany	4.5 Annually	Germany, Hungary
		2.6 ATC-3	Ireland	3.6 Percentage below original (generic price link)	Belgium, the Czech Republic, Greece, Ireland, Italy, Luxembourg, Cyprus, Hungary, Poland, Portugal, France, Austria, Bulgaria, Finland, France, Hungary, Lithuania, Romania, Slovakia, Spain	Austria: 50% lower than the originator, 18% lower than the first generic, 15% lower than the second generic (2020) Slovakia: 45% lower than the originator, 10% lower than the first generic, 5% lower than the second generic (2021) The Czech Republic: 40% lower than the originator (2020) Finland: 50% lower than the originator (2020) France: 60% lower than the originator (2020) Greece: 35% lower than the originator (2020) Hungary: 40% lower than the originator, 20% lower than the first generic, 10% lower than the second generic (2020) Ireland: 60% lower than the originator (2020) Romania: 35% lower than the originator (2020) Spain: 40% lower than the originator (2020)	

Table 19. Payback and Clawback

1. Scope		2. Base for calculations		3. Tax rate	
1.1 Global pharmaceutical target budget	Bulgaria, Poland, Romania, Latvia, Hungary, France, Portugal, Romania, Greece, Italy	2.1 Market share	Finland, Greece, Italy, the UK, Latvia, Hungary, France, Portugal, Romania, Italy	3.1 Part of the consumption excess	Latvia, Italy
1.2 Segmented pharmaceutical target budget	Greece, Italy, Lithuania	2.2 Revenue	Bulgaria, France, the UK	3.2 100% excess consumption	Hungary
1.3 Pharmaceutical expenditure growth rate	Bulgaria, France, Poland, France	2.3 Growth	Bulgaria, Poland, Slovakia, France, Portugal, Italy	3.3 3 thresholds	France
				3.4 100% payback above budget allocation	Romania, Greece
				3.5 70% payback above budget allocation	Portugal
4. Differentiated payback for generics		5. Payback period		6. Payback limitation	
4.1 Yes	Greece, the Netherlands, Romania	5.1 Bi-monthly	Greece	6.1 Limitless	Greece
4.2 No	some European countries	5.2 Quarterly	Latvia, Romania	6.2 Limited	Other European countries
		5.3 Annually	Portugal		

Table 20. Rebates and Discounts

1. Price reduction		2. Country example with various rebates mechanisms	
1.1 ex-factory prices	France (7.5% discount for generics, discount prohibited for brands)	2.1 tendering	the formal procedure to purchase medications using competitive bidding for a particular contract
1.1.2 ex-factory prices for reimbursed medicines	Austria	2.1 a) single supplier tender	the incentive for the supplier to offer the most competitive pricing - the risk of supply issues and drug shortages
1.2 pharmacy purchase prices	Cyprus	2.1 b) multiple suppliers tender	split contracts between suppliers to minimize drug shortages risk
1.3 **price reduction (discount on generics offered by the pharmacy to patients)	UK (discount on generics granted to the patient by pharmacy limited to 17%)	2.1.1 tendering system in the outpatient sector	The Netherlands (preferential pricing policy), Germany, Romania, Latvia
		2.1.1.1 significant use of tendering in ambulatory care	Cyprus, Iceland
		2.1.2 tendering-like models (outpatient)	Denmark, Hungary, Slovakia
		2.1.3 tendering by the sickness funds "Kiwi model"	historical (unsuccessful)
		2.2 negotiations	oftentimes confidential arrangements between two parties (pharmaceutical company and payer)
		2.2.1 individual negotiations in the outpatient sector	Austria, Croatia, Cyprus, the Czech Republic, France, Germany, Hungary, Italy, Norway, Portugal, Slovakia, Slovenia
		2.2.1.1 drugs rebates between sickness funds and individual manufacturers (including generic manufacturers)	Germany, Czech Republic
		2.3 mandatory rebates	Germany, Turkey (for reimbursed drugs representing highly competitive drug classes)

13.2. One-In-One-Out (OIOO)

The EU Commission begun piloting the OIOO in 2021 and has implementation plans scheduled for 2022 (the Commission Work Programme 2022).

Reducing burdens can be done using different techniques according to the Commission:

- Digital tools: to select and reduce specific types of burdens or obligations
- Grouping: to arrange into groups (legislative texts into one volume)
- Reports combining using statistics and consultation mechanisms linked to a few legislative acts coming from the same policy area to create a single obligation
- Responsibility for removal from companies or selected stakeholders for certain obligations and transferring them instead to the public authorities
- Regulations prioritisation over directives due to their immediate impact on all stakeholders
- Legislative replacement⁷⁴

At this point, the European Parliament and the Council still have not made an official statement about the Commission OIOO approach. The EU member states also seem to be divided in the context of OIOO feasibility and effectiveness. Germany, the Netherlands, Denmark, Sweden, Finland, the Czech Republic, Poland, Spain, Hungary, Ireland, Latvia, Estonia, Croatia and Malta for many years have opted for a tool that would allow to loosen the red tape, but once it was finally presented by the Commission it was not received enthusiastically. The mentioned countries stated that this is “too little, too late”.

Three following aspects are mainly criticised:

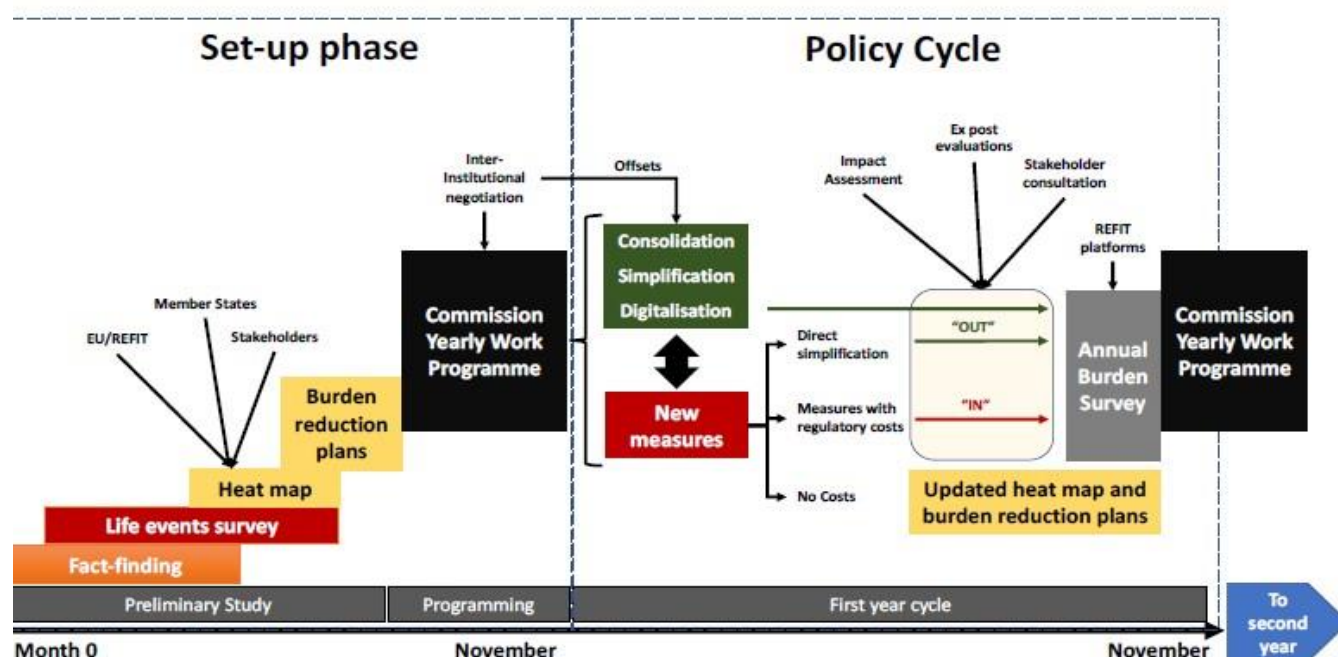
- There is too much flexibility and too many exceptions allowed
- There is not enough information about the internal costs (wages, overheads) regarding new regulations as well as external costs (scientific, accounting or legal assistance and support)
- The adoption of OIOO is too late to be implemented for many legislative proposals that are almost ready for introduction.

Other member states – France, Luxembourg, Belgium, and Bulgaria do not support the OIOO approach due to its unpredictable nature. Additionally, they indicate that OIOO as a tool can negatively impact the quality, consistency, and certainty of the legislative acts adoption process.

The third group of European countries represented by Italy, Romania, Greece, Portugal, Austria, Slovakia, Lithuania, Slovenia, and Cyprus does not have a firm, clear-cut opinion about OIOO. Those countries strongly agree on the necessity of regulatory burden reduction but they would rather use a different tool to achieve this goal.⁷⁴

Step-by-step implementation of OIOO for the EU is proposed along with the plan of burden reduction to help in a systematic manner identify potential “outs”. The implementation would consist of two separate phases – a set-up phase and an annual policy cycle (Scheme 5).⁷⁶

Scheme 5. Step-by-step implementation of OIOO⁷⁶



During the set-up phase, the policy areas that generate the unnecessary costs are identified and extrapolated to a “heat map” (the heat map is updated every year). The issues presented in the heat map are the subject of consultations and the central pillar of the burden reduction plans. In the following phase, in the yearly cycle, the new measures are proposed with consideration of all remarks coming (ad-hoc) from consulted stakeholders. Then the ex-ante impact assessment is performed to indicate “ins” that are expected to replace “outs”. Additionally, the impact assessment should specify timeframes for proposed objectives. The stakeholders’ consultations provide valuable insight related to direct compliance costs. The Annual Burden Survey information collection helps to keep track of what has been already achieved for each policy area by incorporation of measures such as simplification, consolidation, and digitalisation. The survey also enables them to pinpoint what could be added to the anticipated target during the following year.⁷⁶

Weak points of OIOO can be easily identified. Firstly, prior to introducing new regulations – “in” (burdens/ constraints/ regulations), the existing burdens – “out”, need to be indicated and their elimination should be justified. Secondly, for many, OIOO seems to stand in contradiction to the promoted rule of “transparency”. Tertiary, there is a substantial problem with burdens quantification either qualitatively or quantitatively. It is extremely hard to link monetary value with expected results.⁷⁴ Moreover, there is a substantial scepticism regarding the baseline measurements that are not believed to be a cost-effective tool that could be used for significant cost reductions. Baseline calculation is complex and generates costs related to the data availability, transparency, and credibility.⁷⁶

Despite being criticised by some, OIOO meets the criteria of innovative approaches that have been defined in 2016 by European stakeholders, business federations and some member states. OIOO is digital by default, it is “future-proof” and innovation-friendly. Moreover, it has the ability to change the old dynamic by limiting the capacity of the co-legislators to add new obligations that in collective view need to be alleviated.⁷⁴

13.2.1. One-In-One-Out countries’ examples and experiences

Besides some of the EU member states, the UK, the US, Canada, Mexico, and Korea have tried to reduce the rising burdens of new provisions by eliminating the existing ones. In some countries, one-to-one offset (OIOO) was tested, meanwhile, the UK and the US have experimented with one-in-two offset (OIXO). There is also a group of countries that have tried a complementary strategy which entails the establishment of ad hoc burden reduction targets either for all legislation or for selected sectors. The OIXO approach can be counted in practice as well as a direct tool for addressing burden reduction targets.

Out of all 28 countries (after Brexit – 27) in the EU, those countries that represent around 86% of the EU GDP either had (Denmark, the UK), have or will have (Poland, Romania, Slovakia, Slovenia) experience with introducing OIOO/ OIXO. Currently, in 10 member states the OIXO approach is in place (62% of the EU GDP).⁷⁶

Table 21. Countries overview (OIXO)

Country	OIXO model	OIXO scope (costs)	OIXO scope (regulated entities)
Austria	OIOO	Administrative burdens and substantive compliance costs	Businesses and citizens
Denmark	OIOO Discontinued in 2019 by the new government	Administrative burdens and substantive compliance costs	Businesses
Finland	Pilot test (Ministry of Economic Affairs and Employment)	Administrative burdens and substantive compliance costs	Businesses
France	OI2O	Administrative burdens and substantive compliance costs	Businesses, local administration, and services, citizens
Germany	OIOO	Administrative burdens and substantive compliance costs	Businesses
Hungary	OIOO	Administrative burdens and substantive compliance costs	Businesses, citizens, and public administration
Italy	OIOO	Administrative burdens	Citizens and businesses

Country	OIXO model	OIXO scope (costs)	OIXO scope (regulated entities)
Latvia	OIOO	Administrative burdens and substantive compliance costs	Businesses
Lithuania	OIOO	Administrative burdens	Businesses
Poland	Currently planned	Administrative burdens and substantive compliance costs	Businesses
Portugal	OIOO	Administrative burdens	Businesses
Romania	Planned	Planned (no current targets)	
Slovakia	Planned	Administrative burdens	Businesses
Slovenia	Planned	Planned	
Spain	OIOO	Administrative burdens	Businesses
Sweden	OIOO	Administrative burdens	Businesses
The UK	OIOO (2011) OI2O (2013) OI3O (2016) and (2017) (OIXO not in force since 2017)	Administrative burdens and substantive compliance costs	Businesses

It can be inferred that OIXO is at this moment exclusively applied to the business sector in Europe. The majority of countries have positive outcomes, so they are willing to advocate for the OIXO approach adoption by the UE. Countries that are considered regulatory governance leaders have adopted comprehensive programmes for the measurement and reduction of direct costs from regulation, besides other tools used such as public consultation or regulatory impact analysis.⁷⁶

The UK has the most extensive experience in the context of developing and simplifying regulations (see table above) based on a cost and benefit analysis. The Regulatory Policy Committee (RPC) is the British independent entity responsible for costs and benefits validation of all new regulatory and deregulatory proposals. The introduction of OIOO in 2011 in the UK was a spectacular success. Between 2011 and 2012 the targets were not only obtained but also exceeded. The ultimate outcome was the removal of £963 million more in business “out” regulations than was introduced in new “in” regulations.⁷⁶

In the US it is a common practice to combine the OI2O approach with a “stock-flow linkage rule” regarding a volume of incremental regulatory costs. It is obligatory that “any new incremental costs associated with new regulations shall, to the extent permitted by law, be offset by the elimination of existing costs associated with at least two prior regulations”.⁷⁶

13.3. Tax credits

“It eliminates the uncertainty in making R&D investment decisions and serves as a tool for lowering a company's effective tax rate.” – testimonial of R&D company in the US.

There is a largely positive attitude towards the tax credits model in the R&D sector in the US. The tax credits method provides long-term financial relief, encourages investment in the sector and thus stimulates competitiveness.

The UK has followed the US and introduced tax credits for the research and development sector. Only in 2020, over 85 thousand tax credits were made and as the result, £7.4 billion tax relief was paid out. Tax credits are an essential source of non-repayable funding for small, medium, and large companies that either create a new product or develop and modify an existing one. Not only are tax credits associated with “cash injection” that help to thrive and successfully compete on the market, but also, they boost innovation and economic growth. It is estimated that every £1 spent on R&D in the UK generates approximately £7 of net economic benefit to the UK and unlocks £1.40 of private R&D investment.⁷⁹

13.3.1. Examples of tax relief measures in Europe

Spain and Belgium are examples of countries that are willing to reduce taxes (offer tax credits) for pharmaceutical companies in exchange for their extensive investment activities. Since 1998, the Spanish government has supported (PROFARMA program) the pharmaceutical sector to ensure the competitiveness of local medicines manufacturers (the majority of local medicines companies are generic medicines companies). In Spain, pharmaceutical companies are obliged to pay tax which is the equivalent of 1.5-2% of the total value of all reimbursable medicines sold in Spain and their economic impact. Pharmaceutical companies in the PROFARMA program, that have their production and R&D activities set on the Spanish territory, can apply for up to 35% tax exemption. In 2017, 17 Spanish and 21 foreign pharmaceutical firms were eligible for PROFARMA program tax relief. The PROFARMA program participants are additionally supported in their application for financial subsidies offered by the Ministry of Industry, Tourism and Trade. As the result of the long-lasting PROFARMA initiative, the export of medicines has increased as well as the rate of investments in the pharmaceutical R&D sector.⁸⁰

Similarly, in Belgium, the pharmaceutical companies that invested in R&D or decided to apply austerity measures to their excessive spending (between 2006-2016) could have applied for a tax return. The 5% tax return was given 2 years after fulfilling all required conditions by pharmaceutical companies. Until 2018 financial means necessary for tax returns (tax relief package) were secured in the Belgian budget and fully utilised.⁸⁰