



Gesundheit Österreich
GmbH



Euripid Guidance Document on External Reference Pricing (ERP)

Final Version 8.1 of 31 July 2018

DISCLAIMER

This document is part of the project '664317 / Statistical data for medicinal product pricing Euripid' which has received funding from the European Union's Health Programme (2014-2020)."

The content of this document represents the views of the authors only and is their sole responsibility; it can not be considered to reflect the views of the European Commission and/or the Consumers, Health, Agriculture and Food Executive Agency or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information in this document. ."

Authors

Claudia Habl (GÖG)
Peter Schneider (GÖG)

Gergely Németh (NEAK)
Robin Šebesta (SUKL)

Project Assistant

Monika Schintlmeister (GÖG)

This report was produced under the third Health Programme (2014-2020) in the frame of a specific contract with the Consumer, Health and Food Executive Agency (Chafea) acting under the mandate of the European Commission. The content of this report represents the views of the contractor and is its sole responsibility; it can in no way be taken to reflect the views of the European Commission and/or Chafea or any other body of the European Union. The European Commission and/or Chafea do not guarantee the accuracy of the data included in this report, nor do they accept responsibility for any use made by third parties thereof.

More information on the European Union is available on the Internet (<http://www.europa.eu>).

Table of contents

Table of contents.....	III
List of abbreviations.....	IV
1. Guiding Principles Executive Summary	1
1.1. Use of ERP for decision making	4
1.2. Type of price comparison	6
1.3. Scope/Selection of reference countries.....	8
1.4. Scope/Selection of medicines for ERP	11
1.5. Selection of price type	13
1.6. Comparability of pharmaceutical specialities	16
1.7. ERP formula.....	19
1.8. Data sources and Quality	22
1.9. Prices can be adjusted to national requirements.....	25
1.10. ERP needs planning and determined timelines	27
1.11. Transparency of ERP procedures and its inputs	29
1.12. Coordinated European Approach for better ERP	31
2. References	33

List of abbreviations

ATC	Anatomical Therapeutic Chemical
CIF	Cost Insurance Freight
DDD	Daily defined dose
EC	European Commission
ECB	European Central Bank
EMA	European Medicines Agency
ERP	External Reference Pricing
EU	European Union
Euripid	European Price Information Database
GDP	Gross Domestic Product
GD	Guidance Document (i.e. the present document)
GÖG	Gesundheit Österreich GmbH / Austrian Public Health Institute (Austria)
JAZMP	Agency for Medicinal Products and Medical Devices (Slovenia)
HTA	Health Technology Assessment
IPR	Internal Price Referencing
MAH	Marketing Authorisation Holder
MEA	Managed Entry Agreements
MoCA	Mechanism of Coordinated Access to Medicines
NEAK	National Health Insurance Fund (Hungary), formerly OEP
OECD	Organization of economic co-operation and development
PPRI	Pharmaceutical Pricing and Reimbursement Information Network
PPP	Purchasing power parities
SÚKL	Státní ústav pro kontrolu léčiv/ State Institute for Drug Control (Czech Republic)
WHO	World Health Organisation

1. Guiding Principles Executive Summary

The comparison of the prices of medicinal products (i.e. medicines or pharmaceuticals) is an important element of a popular pharmaceutical policy in Europe, known as 'External Reference Pricing' (ERP). Benefits and limitations of regulating prices by the means of ERP have been widely discussed in literature.

Although it has been predicted that the relevance of this policy tool will diminish over the next years [1], it is currently still widely applied in European countries [2, 3] and beyond [4, 5].

This document does neither debate the appropriateness of ERP as pricing policy tool nor promote the use of ERP as price setting tool. The aim of this document is – as defined in the specific objective 3 of the Grant Agreement – to serve as '*a guidance document on a coordinated approach of national authorities regarding the use of ERP to avoid/mitigate negative impact for patient access to medicines*'.

The Euripid Collaboration, with the support of the EU Health Programme¹, jointly developed twelve "Guiding Principles" which are meant to guide a coordinated approach of national competent authorities regarding the use of ERP to avoid/mitigate negative impact for patient access to medicines.

Information on the objectives, members and activities of the Euripid collaboration are available on the homepage of our non-public website: www.euripid.eu

The document was developed, based on a scientific analysis, by a study team of the Euripid Collaboration led by the Austrian Public Health Institute Gesundheit Österreich GmbH (GÖG), the Czech Medicines Agency (SUKL) and the Hungarian National Institute of Health Insurance Fund Management (NEAK) with contributions by Members of the Euripid Collaboration.

The Guidance Document (GD) consists of: a (1) concise overview of the principles in form of an Executive Summary and (2) a more detailed technical background report also explaining the method how the principles were developed. The latter version including the references used is for internal use of the collaboration and EC Services only and will be published on the Euripid intranet.

The Executive Summary is the basis for the laymen version of the Technical Report. The laymen version will take the format of an extended format of the leaflet (cf. <https://www.euripid.eu/aboutus>).

1

Grant No. 664317 / Statistical data for medicinal product pricing EURIPID' which has received funding from the European Union's Health Programme (2014-2020)."

The principles follow the structure: 'Framing the issue – Things to consider – Recommendations'.

- #01) ERP is an important policy tool that should be used in a mix with other instruments and not as stand-alone policy tool.
- #02) ERP should take place on a single product basis rather than by indices.
- #03) The aim of the national pharmaceutical policy should determine the selection of reference countries.
- #04) Evidence has shown that ERP is most effective when applied to pharmaceuticals without generic or therapeutic competition.
- #05) The comparison of prices of medicinal products should be done on the first price (type) in the pharmaceutical distribution chain.
- #06) Competent authorities should apply clear and transparent procedures to determine which pharmaceuticals are considered as comparable.
- #07) The pricing formula applied for ERP should reflect the national pricing policy objective.
- #08) ERP procedures should be performed with the highest possible accuracy and completeness of data sources.
- #09) If price information is adjusted to national requirements, it should be done in a transparent and sustainable manner.
- #10) ERP activities need careful planning and should also be considered as a policy tool for price revisions and monitoring.
- #11) The procedures and price inputs to ERP should be transparent to ensure predictability and effectiveness.
- #12) Policy-makers should consider strengthening their cooperation, in particular through the contribution and benefits of existing policies.

The final document, as published, was prepared following a series of formal and informal consultations including Face-to-Face workshops between Euripid members, further national competent authorities on pricing and reimbursement of medicines, the WHO-PPRI network, European Commission policy officers and stakeholders in the field, i.e. economic operators, professional associations, patient and consumer organisations and third party payers' associations.

The Board of Participants of the Euripid Collaboration endorsed the use of the twelve principles within the remit of their responsibilities.

1

ERP is an important policy tool that should be used in a mix with other instruments and not as stand-alone policy tool.



1.1. Use of ERP for decision making

Framing the issue:

In 2018, ERP (or elements of it) was the most commonly applied pricing policy in European countries: 25 EU countries used ERP, either as the sole or main pricing instrument, or as a supportive criterion in the decision-making process where other criteria (e.g., budget impact) also play a role [6]. Medicines subject to price comparison could be - either on single product basis or for a sample of products - selected by applying different criteria. The aim is to show how ERP can be used in a meaningful way, emphasising synergies with other pricing policies. Recommending the best theoretical pricing policy is outside the scope of this document.

Interdependencies to consider:

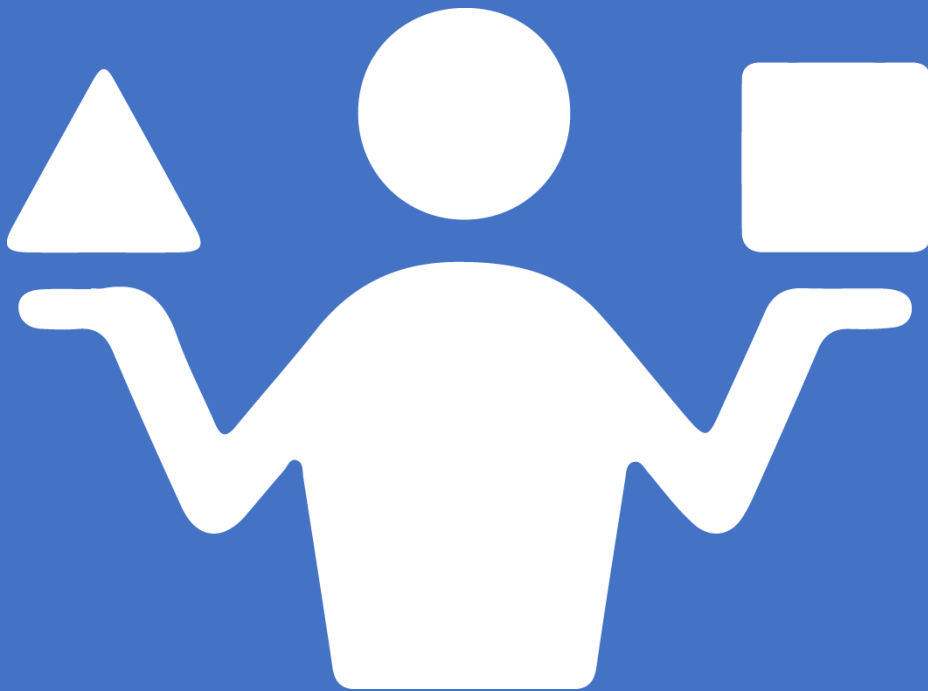
- **Applicability:** The out-patient sector has been the main domain of ERP, although the use of ERP in the in-patient sector is possible and has been implemented in a few countries. Still, the application in the in-patient sector might have some limitations.
- **Utilisation of information:** Because of the limited information available, ERP might not have the capacity required to serve as dominant on-patent pharmaceutical pricing policy. The information collected through an ERP procedure could be used for other purposes, e.g. to check for availability of products in specific markets.
- **Appropriateness of ERP:** While ERP is in principle applicable to a wide range of medicinal products, it should be judged carefully for which type of medicines it takes the best effect (c.f. principle #4).
- **Coordinated European Approach:** Smaller countries may not have the resources to implement an elaborated mix of pricing policies. Regional cooperation/collaboration between neighbouring countries or coordination within the EU could help when setting up a policy mix.

Recommendations:

- ERP is an important policy tool but it should be preferably used in **a mix with other instruments** and not as a stand-alone policy. A balanced comparison of prices should take into account that cross-country differences in prices could be the results of differences in economic and policy terms, such as differences in the burden of disease, health system preferences and ability to pay, patterns of medicines usage (c.f. principle #6), market structures (c.f. principle #9), or distribution chain related components (c.f. principle #5). The use of ERP in a mix with other instruments allows flexibility for the consideration of such differences.
- The price obtained by ERP should not be seen as final, actual price but rather as a **benchmark**.
- **If no other suitable policy tools** are in place, consider the **use of ERP-elements** for regulating prices **in the in-patient sector** - as a benchmark during tenders or to obtain a ceiling price based on prices from other countries.
- ERP can be successfully used as a **supportive criterion** or as a **price limit but should always be complemented by other tools**. Such other tools are for instance, comparisons with available therapeutic alternatives, value-based assessments, negotiations or managed entry agreements and other related non-pricing tools such as budget impact limitation.
- Negotiation power and skills play an important role in the determination of the real prices. International cooperation - as done in Euripid and other joint platforms - has the potential to improve the accessibility of medicines to patients and may enhance the performance of pricing and reimbursement policies and shall thus be enforced.
- In order to deliver the expected outcomes (e.g., increase in access and affordability, ensuring sustainability of availability of medicines, better management of public budgets), it should be carefully considered how ERP fits into the respective health system structure and how it could **interact with other policies**. Always be aware that there is a need for gradual adjustments which could be addressed by respective regulations.

2

ERP should take place
on a single product basis
rather than by indices.



1.2. Type of price comparison

Framing the issue:

Collecting prices of medicinal products and their examination by authorities could have different purposes. Objectives could be (1) to monitor price development, (2) to analyse prices to support HTA and/or reimbursement decisions, or (3) to compare prices. Depending on the purpose, some methods may be more appropriate than others. External price referencing is a form of price comparison by using “*the price(s) of a medicine in one or several countries in order to derive a benchmark or reference price for the purpose of setting or negotiating the price of the product in a given country*” [7].

Literature features two major strands of discussions: (1) comparisons of prices of one (or more) specific medicinal product(s), and (2) comparison of average prices.

The first approach focuses on individual products and is often used by national competent authorities when determining prices at product launch or at the entry into the reimbursement system. The second approach considers the macro perspective by calculating average prices or indices for groups of medicines (e.g. ATC-4 level) or entire markets. While the individual comparison is done on a rather like-by-like basis (i.e. comparing the **same** - or a comparable - medicine defined by pharmaceutical form, dosage and package), the comparison of average prices is usually done by unit (e.g. tablet, capsule, vials) or dosage basis (e.g. a standard unit).

Interdependencies to consider:

- **Role of price comparison:** Awareness whether ascertaining the price level of a given product in one country compared to other countries or the actual determination of the price of a specific medicine is the prime objective of performing price comparison.
- **Availability of information:** Average price comparisons are based on price indices. In order to calculate them, weights could be applied to price information. One of the most common weights applied is volume (e.g., number of items sold in a given time frame in a given country). Check if it is possible to access all necessary information for each type of price comparisons.

Recommendations:

- ERP should take place on **single product² (package) basis** rather than by indices.
- The necessary **personal and technical capacity** must be available to perform the task. If possible, Euripid partners should consult the Euripid database instead of ‘manually’ collecting data from reference countries on a case-by-case basis.
- Price comparison models shall reflect the availability of information in other countries (for instance a ‘Laspeyres Index’ cannot be used if no volume information is available).
- Countries should consider using Purchasing Power Parities for pharmaceuticals³ when comparing price levels (average prices) of substances in the first place.

²

A (pharmaceutical) product is defined as medicine, which is presented and marketed for use with a specific mixture of active ingredients (and inactive ingredients), in a defined pharmaceutical form and apportioned into a particular strength and pack size.

³

cf. a special Eurostat-Euripid Study on the Calculation of Purchasing Power Parities (PPPs) for pharmaceutical products carried out in 2017/2018 (PN5C/06/2016/C4).

3

The aim of the national pharmaceutical policy should determine the selection of reference countries.



1.3. Scope/Selection of reference countries

Framing the issue:

Performing ERP demands information on medicine prices in other countries and the choice of the country basket can be challenging. ERP has been described as a rather 'path dependent' approach for setting prices [8], meaning that the results are to a large extent determined by decisions on methods applied, with the scope of reference countries being one of the major driving factors.

Thus, two major strands of discussions can be found in literature: (1) To include as many countries as possible, and (2) To select a low number of countries.

While (1) aims to mitigate the risk of national prices being influenced by singular price outliers, (2) emphasises the path-dependency of ERP assumptions. The difference between the two approaches lies in the fact that larger country baskets require **more administrative resources to survey price information** from reference countries. In contrast, the second approach may require less administrative staff, but needs to be **carefully considered and tailored to the country specific ERP design** in order to fully materialise the potential of ERP and not produce skewed, and potentially harmful results that might hamper access to medicines. There is no decisive evidence that very large country baskets are more efficient.

Interdependencies to consider:

- **Comparability of the pricing system:** When deciding on reference countries, comparability of the pricing system should be assessed. E.g. countries without regulation of the wholesale remuneration often focus on countries with similar regulations.
- **Fairness:** ERP policies of countries are known to influence marketing decisions of marketing authorisation holders.
- **Market effects:** There are reasonable arguments that ERP tends to incentivise strategic launches and cause substantial delays. However, in practice ambiguous results are observed. In any case, the possible negative impact on accessibility should be addressed on a European level.
- **National up-date frequencies:** Within the EU, pricing and the publication of prices is supposed to comply with EU regulations. However, not all reference countries may have legal provisions on the frequency of price list updates. Also, other pricing policies in place (e.g., regular price freezes) could make regular reviews redundant.
- **Missing Price types** (c.f. principles #8 and #9): Consider the price types (manufacturer price, wholesale price, pharmacy net retail price) that are needed for the application of ERP, when choosing reference countries. Not all price types are available for all countries, neither from national sources nor from Euripid.
- **Administrative burden:** There is a direct proportionality between the number of reference countries and the human resources and technical capacity needed for referencing.
- **Product status:** Dispensation rules of countries could differ for the same product (OTC vs. Rx status, or pharmacy-only, as different add-ons might apply).
- **ERP formula:** Different ERP formulas could be used depending on which countries are included into the ERP basket (e.g. the minimum price approach could be used if countries with similar or higher GDP are in the basket while other approaches could be recommended if countries with lower GDP are in the basket), c.f. principle #7.

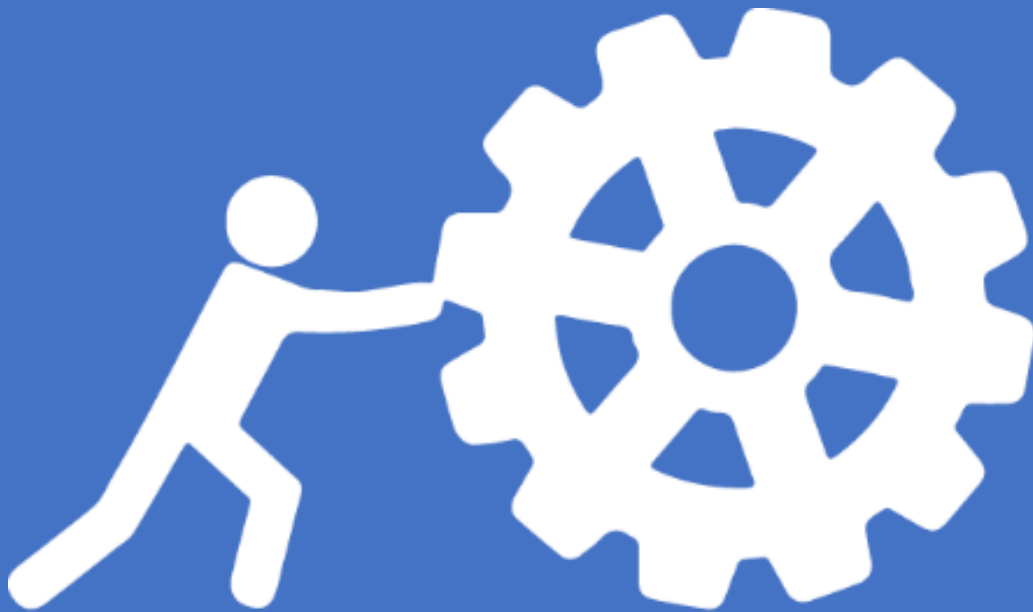
Recommendations:

- Both, smaller or larger country baskets are feasible and manageable alternatives, but simulations suggest that a **smaller, carefully chosen, country basket results** in similar or lower average prices while often requiring less administrative efforts and implies less ramifications to other countries.

- A **careful choice of reference countries** takes into account considerations on economic indicators and indicators related to the performance of the health system as well as aspects of **fairness**.
- The efficacy of ERP as cost-containment strategy does not only depend on the size of a country basket, but also on its **composition and the frequency of price revisions**.
- Consider if the information you need for referencing / comparing is available to you in the necessary format and level of detail; preferably even from Euripid.
- Provide the **appropriate staff resources** to manage the country basket.
- Although low-income countries within the EU are less often included in other EU country's reference baskets, it does not seem to correlate with the likeliness of product launch in the respective country. An **assessment on the potential effects of national ERP on other countries is encouraged** (e.g., in form of a cross-country dialogue platform that could be jointly developed together with stakeholders).
- Competent authorities should **evaluate on a regular basis** (e.g. in the course of a monitoring exercise) the appropriateness of their country basket choice, as part of the reflection process on potential negative aspect of ERP (availability, accessibility, etc.).

4

Evidence has shown that ERP is most effective when applied to pharmaceuticals without generic or therapeutic competition.



1.4. Scope/Selection of medicines for ERP

Framing the issue:

The regulation of pharmaceutical prices varies among countries which have different approaches. These usually reflect national policy priorities and aim to ensure affordable access to medicines for the population, while maintaining financial sustainability and also providing incentives for innovation or supporting domestic production. Therefore, differences in pricing policies are not only related to the mechanisms used to determine pharmaceutical prices, but also to the scope of medicines to which they are applied. With regard to the scope of medicines, theoretically ERP can be applied to all types and categories of medicines and – as literature and surveys show – this is also done by competent authorities. Still, one must be aware that the larger the scope of medicines to which ERP is applied, the more methodological aspects need to be clarified and more administrative resources may need to be allocated to the task. It is also necessary to consider the environment where the product is marketed, i.e. a product might be subject to competition in one country already while it is still under patent protection in another.

Interdependencies to consider:

- **Interaction with other national pharmaceutical policies:** Pricing is embedded in the structure of a national pharmaceutical system. Policy makers should be aware that the effectiveness and results of ERP depend on the interactions with other pharmaceutical policies in place. An example could be HTA or value based pricing. It should be carefully judged whether or not - and to what extent - elements of ERP are applied to generic medicines and biosimilars.
- **Administrative burden:** If ERP is applied to a broader scope of medicines, it will increase the administrative burden.

Recommendations:

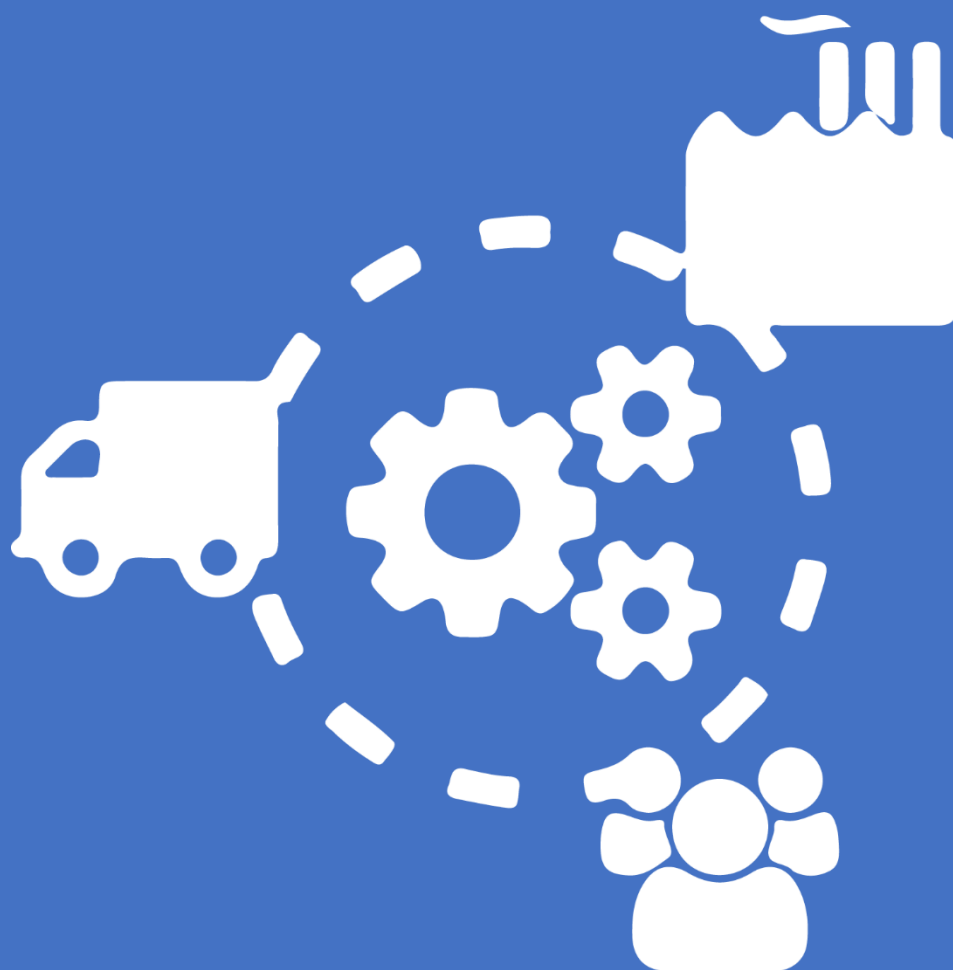
- Evidence shows that ERP takes full effect when it is used for determining **the maximum price of medicinal products without generic or therapeutic competition** independent of the sector through which they are distributed.
- There are **other policies** (e.g., internal price referencing) that **steer or monitor the prices of generics and biosimilars**, which should be taken into account.
- The comparison of price level of products in competitive environments could be used as a benchmark if domestic policies provide sufficient incentives for competition.
- The preferred scope of medicines covered by ERP should be seen in connection with other policies applied in a country or region. A **broader scope of medicines subject to ERP may require more nuanced procedures of ERP**, like the utilisation of ERP-elements together with other measures (e.g. HTA, tenders, value based pricing, internal referencing). In principle, focus should be laid on **prescription-only medicines (Rx)**.
- A possible decision making support, which medicines are eligible for price regulation through ERP used in a mix with other instruments may be provided by **regular monitoring of pharmaceutical expenditures**. Consider the use of decision criteria (e.g. turnover, growth potential, switches) or support techniques like an adjusted-‘ABC analysis’, which is a technique for inventory categorisation and prioritisation⁴.

4

When applying this technique to pharmaceuticals, if the projected sales of a medicine would fall into the group of medicine that account for 80% of TPE, then they are eligible for price regulation through ERP. However, authorities should be aware that the design of such a decision support is flawed, as it provides incentives to MAH to underrepresent their estimations, which could not be controlled due to asymmetry of information

5

The comparison of prices of medicinal products should be done on the first price type in the pharmaceutical distribution chain.



1.5. Selection of price type

Framing the issue:

The provision of medicines is characterised by a supply chain, ensuring the adequate transport from the manufacturer to the patient. As medicines move along the supply chain, costs are added on each stage. As a result of the add-ons different price components (tariffs, duties, wholesale and retail prices, taxes) impact the final price of a medicine. An essential question when designing and applying ERP is the price type which is taken into account for comparison. Since mark-ups or add-ons in the supply chain reflect national priorities in pharmaceutical regulation, the comparison of different price types may lead to inconsistencies.

In theory, ERP can be applied to all price types. Literature and surveys with competent authorities show that in practice it is or has been - in one or the other form - applied to different price types. In Europe the manufacturer price is often chosen because wholesale and retail mark-ups are in most cases statutorily regulated on national level.

Interdependencies to consider:

- **National pharmaceutical policy framework:** When selecting the price type for ERP, national characteristics with respect to pharmaceutical regulation should be considered (e.g. the system of price building).
- **Re-calculation of necessary price types:** National sources or Euripid may not include the needed price type. When mark-ups and add-ons in the reference countries are regulated in a transparent manner, the necessary price type can be recalculated and is partly provided in Euripid (e.g. net/gross retail prices).
- **Approximation of price types:** In some countries certain price types are not available due to the characteristics of the national market.
- **Selection of reference countries** (c.f. principle #3): Eligibility of reference countries could be seen in connection with the selection of price types.

Recommendations:

- ERP should preferably be applied at the **first possible price type, i.e. ex-factory prices**. Margins and taxes are different in the various countries, resulting in varying price differentials along the pharmaceutical distribution chain. Those differences cannot be attributed to the MAH, but to national distributors and to national policies – or in some cases the absence of the latter.
- **Pharmacy purchasing prices** or - from an international perspective - even retail prices can be considered a feasible choice if systemic and economic conditions impede price regulation at ex-factory level. For instance, countries where the retail market is characterised by a large fraction of private expenditures through out-of-pocket payments (OOPP) may have limited manoeuvring room for regulating the pharmaceutical distribution chain. From such a perspective the application of ERP at pharmacy retail prices can be a feasible solution to protect patients from excessive financial burden. There is evidence that high OOPP lead to lower access.
- The **application of ERP at the pharmacy purchasing or retail price level⁵ is more challenging**. In order to ensure comparability of information at this price

5

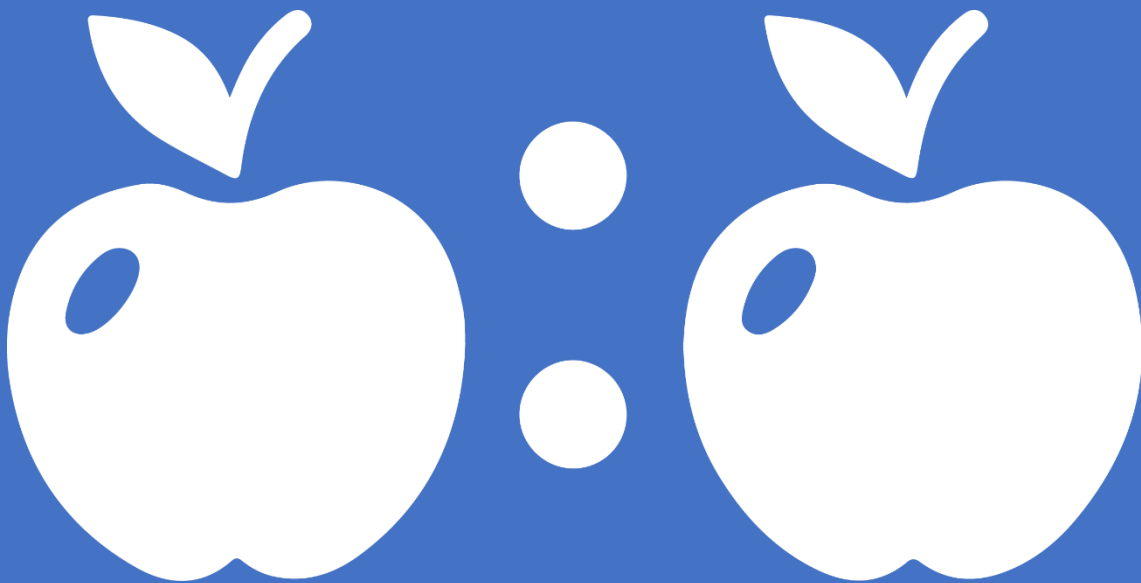
Referencing on retail price level has no relevance for a European setting but is often applied in out-of-pocket countries. Out-of-pocket payments (OOPs) are defined by WHO as direct payments made by individuals to health care providers at the time of service use; which is a typical situation for many Non-EU citizens including the United States residents.

type (c.f. principle #3), more aspects should be taken into consideration and should be accompanied by measures mitigating possible negative effects.

- If **information on the chosen price type is not available in the reference country the country shall be eliminated from the comparison**. If this is not possible, the price could be approximated, e.g. by deducting average add-ons/margins, provided this happens in a transparent manner (meaning that providers of the medicinal product would be given the opportunity to prove the correct price by providing evidence such as wholesale receipts for large quantities). It must be acknowledged that this method results in an indication of the price level, but not an actual price. Approximated prices are currently not provided in Euripid.
- Euripid shall work on adding information to the database that delivers a more complete picture of prices and allows a multi-factor analysis.

6

Competent authorities should apply clear and transparent procedures to determine which pharmaceuticals are considered as comparable.



1.6. Comparability of pharmaceutical specialities

Framing the issue:

Specialities with the same active ingredient can differ with respect to several aspects:

(1) strength, indicating the content and the concentration (if relevant) of an active ingredient expressed per dosage unit, (2) pharmaceutical form, which is the physical characteristic of the combination of active substance(s) and excipient(s) (non-active ingredients) forming a medicinal product, (3) pack size and (4) packaging, with the intention to contain and protect a medicine (which may be in direct contact with it) or helping the administration of the active ingredient to the patient (e.g., with or without needles, applicators, patches).

Differences will also occur regarding the reimbursement a/o patent status a/o the point of service. One crucial question in price comparison is how to deal with medicinal products that are different in one or more of the above stated characteristics. More granular price comparisons may not allow any (or only one) deviation(s), whereas broader price comparisons consider price information of medicines which do not match in even one of the aspects. In literature and also in practice, both approaches can be found, and both approaches have their benefits and limitations. While a narrower price comparison may result in data gaps due to missing price information, the broader price comparison may discourage market launch of therapeutically useful medicinal products due to higher production costs (e.g. paediatric products).

Interdependencies to consider:

- **Linkage to other provisions of the ERP mechanism:** The question of which prices of pharmaceutical specialities are deemed as comparable needs to be jointly answered with questions on other provisions of the ERP mechanism (e.g. data sources, price adjustments).
- **Differences in point of service:** The point of service is subject to the structure of national health system and prices are often determined by different procedures in different sectors, if they are regulated at all. Prices of hospital-(only) products may be relevant but they need to be interpreted with caution, as there is no common definition what constitutes a hospital medicine and the composition of a hospital price might differ across countries.
- **Diverging channels of distribution:** Retail prices of medicines might depend on their distribution channel and could be priced differently depending on national regulation (c.f. principle #5).

Recommendations:

- In the first instance, comparison of prices should be done “like with like”, i.e. between **products with identical pharmaceutical characteristics (active substance(s), strength, pharmaceutical form group and pack size group)**. If prices of products with identical pharmaceutical characteristics are not available, authorities need to carefully consider which pharmaceutical specialities they regard as comparable. The selection criteria for such “back-up” products need to be understandable and transparent and the overall objective why ERP is applied shall be kept in mind (c.f. principle #1).
- In order to account for differences with regard to indications, the ATC code is helpful information. However, authorities should be aware that ATC codes may also be subject to changes or that some countries have developed national variations.
- **Differences in packages of pharmaceuticals** due to differences in containers should be ignored if no therapeutic differences results, as it could incentivise strategic launch activities of medicines with different containers. Differences in packaging due to pack size could be taken into account **by considering unit prices and defining small and large package groups**, and only products within the same group are used for the comparisons of prices.
- **Differences in pharmaceutical forms** for the same active ingredient should be taken into account during pricing and reimbursement procedures if those differences provide additional/different outcomes/health effects or are deemed as therapeutically useful (e.g. paediatric forms).

- Manufacturers should have the opportunity to bring in clinical data that support claims on different outcomes due to packaging or pharmaceutical forms. If relevant these should be considered either at market access of the medicinal product or at price-revision.
- **Develop a comparability catalogue:** National authorities and stakeholders should agree on the clusters of pharmaceutical forms and pack size groups which could be the basis of ERP, preferably on the EU level. Such comparable products could be labelled in Euripid in the long run.
- **Differences in the reimbursement status** of a medicine may be relevant in the decision if a price should be considered during ERP. However, they need to be interpreted against the backdrop of each national pharmaceutical system and possible free-pricing in this market segment. When dealing with differences in reimbursement status careful evaluation is necessary in each case. This also requires detailed knowledge of the reference country's reimbursement regulations.

7

The pricing formula applied for ERP should reflect the national pricing policy objective.



1.7. ERP formula

Framing the issue:

This discussion is sometimes linked to a “fairness”-debate, calling on “richer” countries not to aim for the lowest price. The choice of the formula to determine prices of pharmaceuticals during ERP is very heterogeneous among countries as it is closely linked to pharmaceutical policies’ major objectives: safe and timely access to qualitative medicines, financial sustainability of publicly funded health systems and reward for innovation. The most common formulas are:

- The **Average** (or a slightly modified method) of all medicine prices obtained in reference countries is used as benchmark during pricing procedures
- The **Lowest price** (or a slightly modified method) of all medicine prices obtained in reference countries is used as benchmark during pricing procedures
- **Specific formula:** Countries often have implemented one or more specific requirements in their pricing procedures e.g. prices cannot exceed the highest price in another country

The greatest risk of a “lowest price” formula would be a downward pricing spiral (e.g. when Country A and B are cross-referencing each other) that could decrease prices so much that MAH prefer not to provide Country A and B with the product. Still, literature does not show concrete examples for such situations but simulation revealed this possibility.

Interdependencies to consider:

- **The choice of the ERP formula** is of particular relevance for countries in which ERP is the main criterion during the pharmaceutical pricing process. Competent authorities, who do not use ERP as a sole policy tool seem to be less concerned.
- **The selection of reference countries** (c.f. principle #3) is a major contributing factor that influences prices determined by ERP.
- **Frequency of price comparison:** Irrespective of calculation method, ERP results largely depend on the point in time it takes place.
- **Coordinated European approach:** The ERP formula should be seen in an international context to avoid logic inconsistencies, but also to account for non-availability despite a valid or even centralised marketing authorisation.

Recommendations:

- **“Fairness”** and **“reward for innovation”** shall be carefully considered when determining the ERP formula, and when selecting reference countries (c.f. principle #3).
- If the average GDP per capita of countries in the basket is above the domestic GDP per capita, the **lowest price approach** (or a modified method) could be used, while the **average price approach** (or a modified method) could be applied if countries with lower GDP are in the basket (i.e. average GDP per capita is below domestic GDP per capita).
- The ERP formula **should not aim for a price below the basket’s minimum price.**
- **Exceptional deviations** from the chosen ERP formula due to special conditions are to be taken in a **transparent manner.**
- If ERP formulas are applied to balance the sustainability of systems and ensure a high level of access to medicines, the **average price approach** should be used.
- If ERP formulas are primarily considered to contribute to the control or to the management of public funds, the formula **average of the three lowest prices or lowest price** seems to be most reasonable.
- However, **the ERP formula is only one part of the picture.** Decisions on the calculation method should be taken in conjunction with other – equally important –

factors and ERP should be used in mix with other tools (c.f. principle #1) to ensure access to medicines.

8

ERP procedures should be performed with the highest possible accuracy and completeness of data sources



1.8. Data sources and Quality

Framing the issue:

ERP is usually seen as a simple benchmarking exercise, but the result of the exercise is closely linked with the quality of the inputs that are used in the process. There are several factors, which should be considered when conducting ERP – data sources, transparency (c.f. principle #11), the choice of exchange rate (c.f. principle #9), reference price validity in terms of market availability, accuracy and other factors.

The **role of a 'responsible buyer' has a double mandate**: on the one hand, the aim for cost-containment through efficient use of resources and on the other hand to ensure pharmaceuticals' availability. Referring to prices that have been achieved under certain favorable conditions and are unlikely to be replicated under domestic conditions, could be to the disadvantage of product availability and potentially hamper the access of patients.

Interdependencies to consider:

- **Availability of price information:** Most European countries publish official prices, yet the sources countries use are quite diverse. Their format (analogous or digital), range of products, type of information, and frequency of publishing differs.
- **Topicality:** Countries may not always provide the possibility to look up valid prices for different time periods and/or the information needed to understand the content in-depth.
- **Language issues:** Data display is not standardised and it can be difficult to find a specific product of interest, especially if the information is only provided in the national language.
- **Granularity of information needed:** Obtainable data does not necessarily contain complementary information, such as the market availability of the medicinal product or does not indicate the list price's relevance to a real price of a pharmaceutical product.
- **List prices vs. "real"⁶ prices:** List prices published tend to differ from "real" prices or effective cost to the health systems in many European countries.

Recommendations:

- The most critical parameter is to ensure **timely availability of and access to** a valid source of information on the price type used for ERP in all reference countries.
- MAHs should have the **possibility to challenge determined prices** by proving their claims by documented prices. These documents should refer to a representative amount of the product (e.g., no single purchase order of one unit).
- Information sharing instruments that have been established by public authorities in the field of pharmaceutical pricing and reimbursement, e.g., Euripid database or the PPRI network, should be used to **double-check prices**.
- The rules regarding which medicinal products are subject to ERP and which products are considered as comparable **must be clearly defined in advance** (e.g., it must be defined if parallel traded products can be considered or not).
- Pricing authorities should preferably **refer to prices of products that are available**. National authorities and stakeholders should cooperate to provide reliable

6

In the area of pharmaceutical products, discounts, rebates and managed entry agreements are widespread and are often held to be confidential. As a result, the (published) list prices of medicines do not reflect the prices paid by purchaser and third party payer, which are called 'real' (or actual) prices.

information about the availability of products. For the time being volume information can be considered as proxy for market availability.⁷

- Reimbursement status, patent status, the way of pricing and further similar factors should not be **“hard” criteria** for exclusion of prices found in other countries. They can be taken into account when interpreting the result of ERP (the role of ERP) or when choosing the proper pricing policy mix.

7

Alternative proposal by the Netherlands: Taking into account the limitations of this indicator, volume information can be considered as a proxy cases where there is no clear and up-to-date information provided by the MAH on the availability of products on the national market.

9

If price information is adjusted to national requirements, it should be done in a transparent and sustainable manner.



1.9. Prices can be adjusted to national requirements

Framing the issue:

Prices obtained from reference countries are most likely not readily-comparable and need to be adjusted to fit into the national procedure. Reasons for adjustments might be:

- **Prices are reported in a different currency:** The most obvious reason for adjustment is that prices of medicines are reported in a different currency than the respective national currency.
- **Price types:** Regulation on pharmaceutical prices and distribution chain remuneration vary between countries and ERP applying countries may find themselves in a situation where the relevant price for comparison is not reported/available in reference countries.
- **Pharmaceutical speciality:** Medicines vary due to different characteristics (e.g. pharmaceutical form, dosage) which result in different pharmaceutical specialities.
- **Weighting:** Weights could be applied to prices of pharmaceuticals in order to reflect aspects other than prices like, e.g., consumption or disease prevalence.

Often an adjustment of price information obtained is neither necessary nor desirable.

Interdependencies to consider:

- **Choice of reference countries** (c.f. principle #3): Issues related to conversion or adjusting prices could be avoided or mitigated by carefully selecting countries with the same currency and/or similar health system structure.
- **Fluctuation of exchange rates:** The rate chosen impacts the national ERP result. It is a question with which exchange rate the calculation should be done in case of a price revision as the calculated reference price depends on the exchange rate used and with the change of the exchange rate the reference price can change despite the fact that prices in countries remained the same. It could be considered to introduce a tolerance band as an option to account for fluctuations albeit in many non-EURO countries the fluctuation against the Euro is very low.
- **Comparability of pharmaceutical specialities:** Adjustments to prices are closely related to the question of which pharmaceutical forms are comparable.

Recommendations:

- Due to different national regulations, marketed products and reporting standards, adjusting prices to national requirements is often needed. The adjustment of prices should be done in a **transparent and sustainable manner**.
- An average **exchange rate** of a longer period should be used in order to avoid the effects of exchange rate fluctuation. The average exchange rate of the previous 12 months of the European Central Bank should preferably be used. Countries are not encouraged to adjust their referenced prices only because of currency fluctuations.
- Recalculating **price types** should be preferably based on statutory mark-ups (regarding potential approximation of missing price types c.f. principle #5).
- To compare prices of different pharmaceutical specialities you need to scale prices to a **common denominator**. The utilisation of agreed dose equivalents (e.g. units) seems most appropriate but also (daily) costs of a treatment could be possible.
- In case of **price revisions** via ERP the fluctuation of exchange rates has to be corrected by scrutinising price changes in local currency. A percentage band on tolerable exchange rate fluctuation could be one option. As rule of thumb, the shorter the exchange rate periods, the higher the percentage bands could be.
- If authorities consider a **weighting of prices, it should be done in a reasonable way**. A meaningful application of weights raises the question about data sources and needs to address several aspects. The consideration of economic conditions constitutes a solidarity-based element and requires a political cooperation mechanism.

10

ERP activities need careful planning and should also be considered as a policy tool for price revisions and monitoring.



1.10. ERP needs planning and determined timelines

Framing the issue:

According to the Transparency Directive 89/105/EEC, competent authorities have to publish a list of the medicinal products for which prices have been regulated at least once per year. Decisions need to be made on two relevant points:

- **Period of data collection:** National price lists for medicines are published and/or updated by competent authorities at different intervals. Therefore, the period for data collection has an impact on the availability and validity of price information.
- **Frequency of price comparisons:** Price comparisons for the purpose of ERP can be performed at one or several points of the pharmaceutical's life cycle. Usually ERP comes into play to determine prices at the launch of a medicinal product, but it can also be used at later stages. In some countries, prices of medicines are already published before the assessment by authorities takes place.

In addition, price comparisons could also be undertaken for other purposes than ERP, for instance, price monitoring.

Interdependencies to consider:

- **Data sources and quality:** Prices could be obtained from official sources or MAH. Adjustments to national requirements could go along with the provision of prices by the MAH, but in both cases independent price search or provision of date and procedures should be defined to ensure data quality.
- **Early launch:** When determining the price of a medicine at launch, price information is probably not available in all reference countries. Revisions of ERP-based prices at later periods may contribute to approach the values of the chosen formula.
- **Administrative burden:** The administrative burden depends on the scope of medicines, the number of reference countries and the frequency of price comparisons.

Recommendations:

- **ERP activities should be subject to comprehensive planning and pre-determined timelines.** ERP's potential for being an effective and predictable pricing method depends on time parameters chosen.
- Make the **period of data collection and revision procedures transparent** in order to ensure predictability for stakeholders in the pharmaceutical sector.
- To ensure the most recent prices in European countries, you should align surveying activities with the periods in which prices in reference countries are updated. Among (European) countries there is a wide range of reporting standards including the period and frequency of reporting, but it has been observed that data is often published at the **beginning of a half-year** or the **quarter of a year**.
- Indicate clearly the **validity of price information, and make planned revision timelines transparent**. Since revision schedules in reference countries deviate, price-revising countries may take into account older prices that are about to change.
- The frequency of price comparisons has a nuanced role, depending which purpose they serve. Price comparisons have two major objectives: 1) **revision of prices** and 2) **monitoring pharmaceutical prices evolution** and developments in the pharmaceutical market. Both tasks should be done **annually** with a diminishing frequency for price revision after 36 months of continuous market availability. A **combination of both activities** would allow authorities and companies involved in revision a/o monitoring to benefit from 'economies of scope'. The use of Euripid database simplifies regular monitoring activities.

11

The procedures and price inputs to ERP should be transparent to ensure predictability and effectiveness.



1.11. Transparency of ERP procedures and its inputs

Framing the issue:

Transparency in the context of ERP is related to the following aspects:

- **Procedures:** Rules for the choice of the reference products need to be clearly described, regarding e.g., non-reimbursed pharmaceuticals, out-patient/hospital-only pharmaceuticals, different pack size, different dosages or different pharmaceutical forms.
- **Inputs:** A pre-requisite for applying ERP is the availability of information on pharmaceutical prices, since having at least one data point is a '*conditio sine qua non*' for any comparison. Price information on regulated and/or reimbursed medicines is included in national price lists, but their informational content may vary.

It is important that the applied procedures and inputs are **published in its completeness**, and also the **formula to determine** the reference price is made transparent.

Although both aspects are of major relevance, the discussion seems to mainly focus on price inputs as discrepancies between the prices included in public price lists ('list prices') and the prices actually paid by a third party payer ('real prices') seem to have increased in the last couple of years.

Interdependencies to consider:

- **Role of ERP:** A major source of critique is related to the role of ERP in price decisions. ERP is an important policy tool, but it is not a magic bullet that will meet all expectations regarding access and affordability. It should be used in a mix with other tools and not as a stand-alone policy and its role and the interplay with other policies should be transparent.
- **Pharmaceutical policies:** Objectives of pharmaceutical policies (e.g., availability of medicines, sustainable prices, prevention of depletion of market, avoidance of delays in launching) can be, for pragmatic reasons, in conflict with transparency requirements in an international context. Questions on price transparency and ERP activities should be evaluated and answered in their entirety).
- **Coordinated European approach:** With respect to pharmaceutical pricing, Council conclusions suggested to give consideration to 'improved cooperation on building mechanisms for **increased transparency** and better coordination to minimise any unintended effects that current national pricing systems may have in terms of accessibility throughout the EU [9].

Recommendations:

- Stakeholders and competent authorities in the field of pharmaceuticals should **commit to transparency** as it increases accountability and could contribute to an improved coordination of ERP activities on European level. Countries and stakeholders should jointly establish a Dialogue Platform for these topics.
- Once determined procedures and input generation models shall be critically evaluated from time to time but not too often, to ensure a **sustainable and predictable environment** for all actors in the system. The Euripid database is a stable source for input available to authorities, and trainings are provided by the Collaboration.
- Any pricing policy can be judged by its predictability and efficacy. The more transparent both, procedures and price inputs, are, the more predictable and efficient the results will be. Authorities shall **provide additional information on how prices are determined** (e.g., which products and prices were considered, methods).
- Procedures shall contain provisions that allow manufacturers (MAH) to challenge or appeal reference prices that seem to be calculated incorrectly, perhaps even before official publication by authorities.

12

Policy-makers should consider strengthening their cooperation, in particular through the contribution and benefits of existing policies



1.12. Coordinated European Approach for better ERP

Framing the issue:

The European competent authorities for pricing and reimbursement (CAPR) have remit to make administrative decisions on pricing and/or reimbursement, bestowed on them by national legislation, and the European collaboration platforms listed further are often accessible solely by competent authorities, although some of them enable stakeholders to participate. This principle describes the continuum of cooperation, maps ongoing initiatives and explores the pre-requisites for a coordinated European approach on ERP.

Interdependencies to consider:

- Pricing and reimbursement remain **national competencies**: Still, there are numerous possibilities for national authorities to cooperate or get involved through a joint approach.
- The ERP tool can be enhanced either indirectly (with a decision whether or not to apply it vs. other pricing policy options, and if yes, with a decision when and how to apply or when and how not to apply it) or directly (methodology, availability and quality of inputs, algorithms, outcomes and impacts).
- **State of the art ERP requires more information than just a price**; nevertheless, any ERP methodology should rest on available and traceable data on prices in the referenced Member States.
- **EU-level legislative** framework stipulating an upfront presence of criteria (i.e. methodologies), compliance to timelines and possibility of appeal exists (“Transparency Directive”).

Recommendations:

- **Maintaining and deepening cooperation** between countries in platforms like the CAPR Network, Pharma Policy Directors’ Meetings, PPRI etc. is helpful to obtain general information on other countries. It should be complemented by a **Dialogue Platform** with stakeholders - such as established in Euripid – for exchange of information.
- Strengthen cooperation in a cluster of countries like BENELUXA⁸, V4+, La Valletta etc. is a way forward for any competent authority providing a more active approach through engaging in a **dialogue with other authorities and stakeholders** (e.g. as in the MoCA exercise); it can also be a way to complement or replace an ERP system.
- **Closer cooperation of bodies building up or maintaining cross-country databases** in the field of medicines and access to them (e.g., Euripid, EMA Art. 57 database, WHO) thus completing the information available for decision makers, providers, health professionals and patients. In the long run medical devices could be integrated in a stepwise approach.
- Participation in a project like Euripid is helpful to obtain not only prices of medicinal products, but also to get more detailed information on other countries relevant to prices and necessary to maintain and operate ERP system.
- The **importance of cooperation between each competent P+R authority and pertinent regulatory authority** in ongoing European projects should not be forgotten. Connecting the two processes, which in the past were principally sequential, can contribute to early access of innovative medicines to patients.

8

The Beneluxa Initiative on Pharmaceutical Policy consists of Belgium, The Netherlands, Luxembourg, Austria and Ireland. The Initiative aims to ensure sustainable access to innovative medicine at affordable cost for its patients.

- Competent authorities of EU/EEA Member States should **share any additional information relevant to prices** - *in compliance with applicable national and contractual confidentiality provisions* – in view of their impact on the functioning of the market, especially information on product availability in a certain country.
- Competent authorities could explore pre-requisites to **share any currently restricted information relevant to prices** referred to in the previous item within existing platforms that are currently operating with a restricted access to data, such as Euripid, in a step wise approach. It is advised to explore coordination in the area of pharmaceutical product pricing, particularly with regard to sharing of ‘real prices’ and how they can be implemented in pricing procedures.
- **Developing meaningful indicators:** Coordination on health policy within the EU can only be achieved voluntarily by national competent authorities. Such a coordination effort requires **reliable and updated information** on other European countries to enable joint informed decision making. Regular reporting, systematic monitoring and information sharing is the backbone of coordination.
- Therefore a **monitoring group** within the collaboration should be established, to develop meaningful indicators and to keep track of changes in national pricing and reimbursement systems.

2. References

See also the Technical Guidance Document Full Report.

- [1] Seiter A. A practical approach to pharmaceutical policy. World Bank Publications, 2010. Report No.: 0821383876
- [2] Toumi M, Rémuzat C, Vataire A-L, Urbinati D. External reference pricing of medicinal products: simulation-based considerations for cross-country coordination. Final Report. European Commission, 2014.
- [3] Vogler S, Lepuschütz L, Schneider P, Stühlinger V. Study on enhanced cross-country coordination in the area of pharmaceutical product pricing. European Commission, Directorate-General for Health and Food Safety Ed.; Brussels: Publications Office of the European Union 2016.
- [4] Babar Z-U-D. Pharmaceutical prices in the 21st century. Cham, Switzerland: Springer. 2015.
- [5] Babar Z-U-D. Pharmaceutical Policy in Countries with Developing Healthcare Systems. Springer International Publishing AG; 2017.
- [6] Pharmaceutical Pricing and Reimbursement Information (PPRI). <http://whocc.goeg.at/About/PPRI>: WHO-Kooperationszentrum für Arzneimittelpreisbildung und -erstattung, accessed 5. Mai 2013.
- [7] WHO Collaborating Centre for Pharmaceutical Pricing and Reimbursement Policies. Glossary of pharmaceutical terms. Update 2016. Vienna: Gesundheit Österreich GmbH (GÖG), in coordination with the Pharmaceutical Pricing and Reimbursement Information (PPRI) network and the World Health Organization (WHO), 2016.
- [8] Kanavos P, Nicod E, Espin J, Van Den Aardweg S. Short-and long-term effects of value-based pricing vs. external price referencing: EMiNet; 2010.
- [9] European Commission. Communication from the Commission: On effective, accessible and resilient health systems. Brussels: European Commission; 2014.