PAYER POLICIES TO SUPPORT INNOVATION AND ACCESS TO MEDICINES IN THE WHO EUROPEAN REGION

OSLO MEDICINES INITIATIVE TECHNICAL REPORT

Sabine Vogler
Oslo Medicines Initiative

Established in 2020, the Oslo Medicines Initiative (OMI) is a collaboration between the WHO Regional Office for Europe, the Norwegian Ministry of Health and Care Services and the Norwegian Medicines Agency. The OMI aims to provide a neutral platform for the public and the private sectors to jointly outline a vision for equitable and sustainable access to and affordability of effective, novel and high-priced medicines.

In line with the Regional Office’s European Programme of Work 2020–2025 – “United Action for Better Health”, equitable and sustainable access to quality medicines is critical for universal health coverage and for achieving the Sustainable Development Goals. The OMI provides a strong focus on equity and on leaving no one behind, and is underpinned by three pillars; solidarity, transparency and sustainability.

The OMI has commissioned a series of technical reports to summarize relevant evidence and provide policy considerations as a basis for discussion to inform its work. These reports are also in line with the implementation of World Health Assembly resolutions, in particular resolution WHA 72.8 on improving the transparency of markets for medicines, vaccines, and other health products.
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Sabine Vogler
Abstract

This Oslo Medicines Initiative technical report presents existing policy options for payers that support innovation and access to medicines in the WHO European Region. It identifies innovation incentives, such as early assessment schemes, managed entry agreements and dedicated budgets (so-called innovation funds), across 48 countries in the Region. These incentives are supplemented by supporting assessment tools to generate evidence for informed decision-making (such as horizon scanning and health technology assessments) and access policies for innovation, such as value-based pricing, pooled procurement and subscription fee-based procurement. The report also points to possible limitations of the identified policies; some innovation policies can challenge the financial sustainability of health-care systems, and there are trade-offs between incentivizing innovation and principles of evidence generation, transparency and budget impact. Case studies demonstrate how two countries apply a mixture of policies to support innovation and access to medicines.

Keywords

INNOVATION, ACCESS TO MEDICINES, PHARMACEUTICAL POLICIES, PRICING, REIMBURSEMENT, HTA, PROCUREMENT
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This report was authored by Sabine Vogler (Pharmacoeconomics Department, Gesundheit Österreich [Austrian National Public Health Institute]).

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The author would like to thank members of the Pharmaceutical Pricing and Reimbursement Information (PPRI) network of competent authorities who have shared information on pharmaceutical policies in their countries for several years, with the aim of informing colleagues in the network and allowing dissemination of defined data by the PPRI Secretariat (hosted by the author’s institution). Updated comparative country policy information in this report is mainly sourced from the PPRI network, in addition to published literature.

This technical report is supplemented by a country case study on Italy, available in accompanying web-annex. The author is grateful to Nicola Magrini, Simona Montilla, Agnese Cangini, Enrico Costa, Giuseppe Traversa and Francesco Trotta (Agenzia Italiana del Farmaco (AIFA) [Italian Medicines Agency]); Vincenzo Rebba (AIFA Pricing and Reimbursement Committee and University of Padua); Anna Maria Marata (AIFA Scientific Technical Commission and Region Emilia-Romagna); Francesco Nonino (Region Emilia-Romagna); and Annalisa Campomori (AIFA Pricing and Reimbursement Committee) for their input and review to support the development of the country case study on Italy.

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## Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tbody>
<tr>
<td>AIFA</td>
<td>Agenzia Italiana del Farmaco [Italian Medicines Agency]</td>
</tr>
<tr>
<td>AMNOG</td>
<td>Arzneimittelmarktnovorungsgesetz [Act on the Reform of the Market for Medicines] (Germany)</td>
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<tr>
<td>AMR</td>
<td>antimicrobial resistance</td>
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<tr>
<td>ATU</td>
<td>Autorisation temporaire d’utilisation [temporary authorization for use] (France)</td>
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<tr>
<td>CDF</td>
<td>United Kingdom Cancer Drugs Fund</td>
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<tr>
<td>DRG</td>
<td>diagnosis-related group</td>
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<tr>
<td>EAMS</td>
<td>United Kingdom Early Access to Medicines Scheme</td>
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<tr>
<td>EU</td>
<td>European Union</td>
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<tr>
<td>G-BA</td>
<td>Gemeinsamer Bundesausschuss [Federal Joint Committee] (Germany)</td>
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<tr>
<td>GRADE</td>
<td>Grading of Recommendations, Assessment, Development and Evaluation [methodology]</td>
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<tr>
<td>HTA</td>
<td>health technology assessment</td>
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<tr>
<td>ICER</td>
<td>incremental cost–effectiveness ratio</td>
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<td>IHSI</td>
<td>International Horizon Scanning Initiative</td>
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<tr>
<td>LIS/HINAS</td>
<td>Legemiddelinkjøpsamarbeidet [Drug Procurement Cooperation] / Helseforetakenes Innkjøpservice AS [Health Trusts’ Purchasing Service] (Norway)</td>
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<tr>
<td>MEA</td>
<td>managed entry agreement</td>
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<tr>
<td>NHS</td>
<td>National Health Service</td>
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<tr>
<td>NICE</td>
<td>United Kingdom National Institute for Health and Care Excellence</td>
</tr>
<tr>
<td>NUB</td>
<td>Neue Untersuchungs- und Behandlungsmethoden [New diagnostic and treatment methods] (Germany)</td>
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<tr>
<td>OMI</td>
<td>Oslo Medicines Initiative</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
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<tr>
<td>--------------</td>
<td>-------------</td>
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<tr>
<td>PPRI</td>
<td>Pharmaceutical Pricing and Reimbursement Information [network]</td>
</tr>
<tr>
<td>R&amp;D</td>
<td>research and development</td>
</tr>
<tr>
<td>QALY</td>
<td>quality-adjusted life-year</td>
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<tr>
<td>SPMS</td>
<td>Serviços Partilhados do Ministério da Saúde [Shared Services of the Ministry of Health] (Portugal)</td>
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<td>VBP</td>
<td>value-based pricing</td>
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Executive summary

Background

Access to safe, effective, quality-assured and affordable essential medicines is critical for achieving universal health coverage and the Sustainable Development Goals. Nevertheless, high prices restrict access to potentially effective novel medicines; and areas of unmet medical need exist for which no treatment options are currently available. Policy action is needed to incentivize the development and market entry of novel medicines, and to ensure access to medicines for patients without compromising the sustainability of publicly funded health systems.

Objectives and approach

This report presents and discusses payer-focused policy options that support innovation and access to medicines in the WHO European Region. It identifies innovation policies across 48 countries in the Region, highlighting examples of policy implementation and discussing them in the light of the principles of the Oslo Medicines Initiative (OMI). This comparative analysis is supplemented by two country case studies. The paper focuses on pharmaceutical policies in the peri-launch phase: policies in the areas of pricing, procurement and reimbursement of medicines that aim to manage inclusion of medicines in the public health system and – in the context of this paper – to incentivize the launch and appropriate uptake of pharmaceutical innovation.

This review is based on publications and – to an important extent – unpublished information on country pharmaceutical policies shared by competent authorities represented in the Pharmaceutical Pricing and Reimbursement Information (PPRI) network. The review does not consider other economic incentives offered to companies through policies intended to stimulate technological innovation and growth.

Findings and policy considerations

No globally accepted definition of the term “pharmaceutical innovation” exists; and there is variability in definitions between countries – when they do exist. Key components of pharmaceutical innovation are usually its ability to address unmet medical need and its added therapeutic value.

This review identified 12 types of payer-focused instruments and policies in the Region applied to innovation and access to medicines. Two are assessment tools that generate
evidence on the degree of innovation – including the added value of the medicine – to inform pricing and reimbursement decision-making.

- **Horizon scanning** is a methodology that identifies high-value candidates of pharmaceutical innovation in research and development (R&D) pipelines in order to alert health-care systems.

- **Health technology assessment (HTA)** is an instrument used to assess a medicine in terms of its (added) therapeutic value and possible further benefits and impacts; it thus provides an evidence base for decision-makers on the price and coverage of a medicine.

The remaining policies include six types of innovation incentives and four access policies for innovation.

- **Early access schemes** allow market entry and sometimes inclusion in public funding of medicines that have not yet been granted marketing authorization.

- **Managed entry agreements** (MEAs) are contractual arrangements between the public authority payer and the pharmaceutical company on the price and conditions for inclusion of the medicine in public funding. They can be financial or performance-based, and are usually accompanied by confidential provisions, such as discounts.

- **Free pricing** denotes a lack of price regulation; this allows pharmaceutical companies to determine the medicine price at their own discretion.

- **Innovation funds** are additional funding sources for defined (innovative) medicines – for example, for specific indications such as cancer – outside the standard pricing and reimbursement policy framework.

- **Diagnosis-related group carve-outs** are also additional funding sources to pay for specific (innovative) medicines used in hospitals on an individual product basis. They stand in contrast to the bundled funding scheme of diagnosis-related groups used as a standard for hospital funding, in which medicines are not remunerated separately.

- **Exemptions from payments to payers** include exemptions from and reductions of statutory payments by pharmaceutical companies to public payers (including mandatory discounts, paybacks or clawbacks stipulated in legislation, not in individual contracts).

- **Value-based pricing** is a policy in which pricing and reimbursement decisions for a medicine are completely integrated, based on the value assessment provided by HTA.

- **Pooled procurement** involves increasing volumes and strengthening bargaining power by purchasing jointly through a permanent procurement body or a collaborative agreement.
- **Subscription fee-based procurement models** grant a predefined fixed award to pharmaceutical companies in return for their supply of medicines.

- **Policies for biosimilar medicines** are demand-side measures targeted at doctors and pharmacists to encourage them to prescribe and dispense biosimilar medicines, thereby increasing their use.

In addition, **collaborative approaches** can be applied to support innovation and access to medicines, both within a country (via vertical collaboration between regulatory authorities, HTA bodies and payers) and across countries. The latter can include technical collaborations on methodologies and tools (such as horizon scanning or HTA) and joint procurement of medicines.

Policies commonly used in the WHO European Region are HTA and MEAs; policies to encourage uptake of biosimilar medicines and pooled procurement models are used, but to a lesser extent.

The case studies demonstrate how two countries apply a mixture of policies to support innovation and access to medicines. **Italy** introduced innovation funds, which confer financial benefits for medicines that meet eligibility criteria. These augment the country’s widespread, long-term use of MEAs and early access schemes for non-authorized medicines. Incentives to encourage early access to new authorized medicines are a major feature of the pharmaceutical policy framework in **Germany**. Once a medicine receives marketing authorization, it can be launched on the German market at a price determined by the pharmaceutical company. An HTA is conducted during the first year as a basis for negotiations on the price that will be reimbursed from the thirteenth month. If the negotiated reimbursement price is below the price charged during the first year, no payback is required from the company.

The findings highlight that countries in the Region have developed payer-focused policies to encourage innovation. Sometimes a policy advances one objective at the expense of other goals, however. In particular, policies that **incentivize innovation** may conflict with policies that aim to **ensure affordable access** to medicines, as some innovation policies – particularly incentives granting exemptions from rules and additional funding for pharmaceutical companies – can challenge the sustainability of health systems. In their current design, some incentives (for example, MEAs comprising confidentiality clauses, and access to additional funds despite limited evidence and/or a negative HTA recommendation) are not aligned with the principles of transparency and solidarity, which are pillars of the OMI.

Policy-makers may mitigate some negative implications and consequences of innovation incentives through special features in the design of the policy. To achieve this, clear and transparent criteria defining eligibility for these incentives are beneficial; these help target innovation that could be more precisely addressed by incentives. Another policy option to reduce negative consequences is to **attach conditionalities**. For example, incentives may be granted only if pharmaceutical companies share necessary data with the authorities (such as the contribution of public R&D funding of the medicine, all clinical trials results including negative ones, and net price and volume data in other countries).
Application of HTA and horizon scanning assessment tools can support aligning the potentially conflicting objectives of innovation and affordable and sustainable access, as they generate evidence and offer an assessment of the medicine for various dimensions. They provide guidance to policy-makers on whether – and under which conditions – a medicine may be privileged and granted incentives. This also stresses the relevance of the mixture of policies and tools, as policy-makers benefit from assessing the totality of incentives and the impacts of these policies instead of considering single policies in isolation.

Both collaboration between national authorities across the pharmaceutical value chain and cross-country collaboration have the potential to improve affordable access to novel medicines because the capacity of public authorities is strengthened by sharing knowledge, expertise and data, improving their negotiation power. Given the trade-offs and the different perspectives of health and industrial policy, coordination between government departments for health and industrial policy can thus help to align conflicting policy objectives of innovation and access.

As the legal and organizational set-up of pharmaceutical systems vary across countries, it is helpful to analyse the local context before introducing any new measures. This allows the policy design to be adjusted for the national setting. It is also important that policy-makers monitor and evaluate innovation policies once implemented to facilitate adaptation, where needed.
Introduction

1.1 Background

Access to safe, effective, quality-assured and affordable essential medicines is critical to achieving universal health coverage and the Sustainable Development Goals (1–3). Several governments, including those of high-income countries in the WHO European Region, have increasingly expressed concern about prices that restrict access to potentially effective novel medicines (4). Furthermore, several areas of unmet medical need, for which no treatment options are currently available, still exist. For instance, an effective therapy is lacking for 95% of the over 7000 rare diseases, including rare cancers (5). A prime example of unmet medical need is antimicrobial resistance (AMR), which is a major public health problem, accounting for numerous deaths and complications in treatment (6, 7).

In addition to stewardship measures to reduce excessive and inappropriate use of antibiotics, there is a need for novel antibiotics that have lower probability of resulting in AMR (8).

Appropriate policy action is needed to incentivize the development and market entry of novel medicines, and to ensure access for patients without compromising the sustainability of publicly-funded health systems. This requires coordination at the governmental level.

From a toolbox of options, policy-makers can select the most appropriate pharmaceutical policies to meet the objectives of their country context. Pharmaceutical policies differ in their intended purposes – for example, cost-containment policies aim to ensure financial sustainability; innovation policies aim to incentivize the development, production and market launch of pharmaceutical innovations; and assessment tools aim to help prioritize and/or determine the value of medicines. Some policies may address more than one objective, and this may lead to challenges if objectives are conflicting (such as rewarding developers and producers for innovation versus the need to generate savings for public budgets) (9).

Pharmaceutical policies are implemented at different points in the lifecycle of a medicine (the value chain) (10,11):

- before marketing authorization, at which a medicine demonstrates its safety, effectiveness and quality (pre-launch phase);
- between marketing authorization and market entry of a medicine (peri-launch phase); and
- after market entry (post-launch phase).

In the peri-launch phase, major decisions need to be made on the price at which a health system can, and is willing to, purchase and include the medicine in its benefits package scheme. Appropriate selection of pricing, procurement and reimbursement policies and
supporting tools such as health technology assessment (HTA) is crucial. Policy options to encourage innovation and access to medicines are frequently – but not always – price-related. Further innovation policies may also address other triggers, such as incentivizing the use of specific medicines, accelerating time to market, increasing revenue for pharmaceutical companies or allowing a lower level of evidence (12,13).

In recent decades, several comparative overviews of pharmaceutical pricing, procurement and reimbursement policies used in countries in the Region have been published (10,14–16). A number of studies, including another technical report for the Oslo Medicines Initiative (OMI), have also documented how several of these policies have contributed to supporting access to medicines and affordability (10,11,15,17,18). Suggestions about how to support pharmaceutical innovation have been made in academic and policy debates. These proposals frequently relate to incentives to encourage research and development (R&D), including discussion of new business models, as developed in another OMI technical report (19). Some of these have been piloted, while others are still under discussion. Fewer publications have studied peri-launch policies related to pricing, procurement and reimbursement as possible options to encourage market entry of pharmaceutical innovation, and these have mainly focused on high-income countries (12,20). However, an up-to-date repository of payer-focused pharmaceutical policies (including possible experiences with these policies) used by countries in the Region to support innovation and access to medicines is lacking. This technical report aims to address this gap.

1.2 Key concepts

1.2.1 Pharmaceutical innovation

A clear, globally-accepted definition of pharmaceutical innovation (or of innovative medicines) is lacking. Major components to define innovation are unmet medical need and added therapeutic value (that is, enhanced effectiveness in relation to competitors) (20) as well as novelty (of structure or mechanism of action) (21). Whether the concept of innovation can be operationalized as incremental or a matter of degree has been much discussed, since the level of innovation is considered in pricing and reimbursement decisions in several countries (22). To account for the variation, different terminology is used: for example, Garner (23) distinguishes between discrete innovation, which produces a completely new health technology, and incremental (or continuous) innovation, which consists of several steps of improvement and modification. Morgan et al. (24) use a three-level approach to categorize innovation as incremental, substantial or radical (or breakthrough), depending on the health needs addressed and the comparative effectiveness.

This technical report focuses on innovation policies that are able to foster breakthrough innovation (also called discrete or real innovation). It should be noted, however, that incremental innovation is also important and needs to be encouraged. For ease of readability, the paper uses the term innovation to refer to both discrete and incremental innovation.
1.2.2 Access to medicines

Access has been defined as “the patient’s ability to obtain medical care, including medicines, and a measure of the proportion of a population that reaches appropriate health services, including medication” (25). Affordability and availability are two key factors to determine access (26,27), but others exist.

Affordability relates to the extent to which medicines (and health technologies) are provided to people who need them at a price either they or their health system can pay. Thus, affordability is determined by both the price offered (supply side) and the ability of the purchaser to pay (demand side).

Availability refers to the actual provision of the medicine to patients. Several barriers to availability exist.

- The needed medicine may not yet have been developed and authorized.
- The pharmaceutical company may not have launched it because some markets are not attractive (such as low-income countries or small markets).
- A medicine may be launched with delays due to widespread use of external reference pricing (a pricing policy in which medicine prices in reference countries are used as a benchmark for setting the price); this may cause staggered market launch, with delays in countries with lower price levels (28,29).
- Shortages may occur as a result of disruptions in the supply chain, and medicines may be withdrawn for safety or commercial reasons (for example, repurposing medicines by developing new formulations of the same medicine to be marketed at higher prices (30)).

1.3 Objective

This technical report presents and compares policies for payers – particularly in the areas of pricing, procurement and reimbursement – that aim to support innovation and access to medicines in countries in the Region. Since policies are defined as “instruments, tools and approaches that allow policy-makers to achieve defined objectives” (25), strategies employed by the private sector are not considered policies and are not within the scope of this paper. Policies employed in both the outpatient and inpatient sectors are considered. Pricing and reimbursement policies are typically created and applied by individual countries (Member State competence).

This technical report was produced as part of the OMI, developed by the WHO Regional Office for Europe in collaboration with the Norwegian Ministry of Health and Care Services and the Norwegian Medicines Agency, which aims to find solutions to ensure better access to effective, novel, high-priced medicines (31). The paper explores pharmaceutical policies in the areas of pharmaceutical pricing, procurement and reimbursement; it does not include incentives for R&D, as these are addressed in other OMI technical reports – in particular, those by Moon et al. (19) and Mestre-Ferrandiz et al. (32). It also builds on the OMI technical report by Docteur (18), which discusses selected policies in terms of their ability to support access – in particular, affordability. The review does not consider other economic incentives offered to companies through policies intended to stimulate technological innovation and growth (33).
To map policies in countries in the WHO European Region, a literature review was undertaken; it included both peer-reviewed papers and unpublished grey literature and documents. The latter included information and data collected from the Pharmaceutical Pricing and Reimbursement Information (PPRI) networks managed by the Austrian National Public Health Institute (34,35). The findings of a validation of national pharmaceutical policy frameworks conducted with PPRI network members at the end of 2021 (a recurrent PPRI activity, independent of this paper) also provided updated data. The information presented in this paper relates, as far as possible, to 2021.

At the time of the survey, the PPRI network comprised public authorities responsible for pharmaceutical pricing and reimbursement in 52 countries, of which 43 are in the WHO European Region. In addition, the regional PPRI Eastern Europe and Central Asia (EECA) network comprises 12 countries in eastern Europe and central Asia, including five that are not members of the larger PPRI network. These PPRI networks cover 48 of the 53 countries in the Region, and this paper presents information on those countries (Albania, Armenia, Austria, Azerbaijan, Belarus, Belgium, Bulgaria, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, France, Georgia, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Luxembourg, Malta, Netherlands, North Macedonia, Norway, Poland, Portugal, Republic of Moldova, Romania, Russian Federation, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Tajikistan, Türkiye, Turkmenistan, Ukraine, United Kingdom and Uzbekistan).

Two country case studies are also provided to demonstrate the application of a mixture of pricing, procurement and reimbursement policies aiming to support innovation and access to medicines. The case studies were based on the available literature. A separate detailed report was produced for the Italian case study, and its findings were shared with public authorities in the country for review, comment and validation. It is available as accompanying web-annex.

In addition, information on cross-country collaboration was collated, based on the literature and previous research by the author.
POLICIES TO SUPPORT INNOVATION AND ACCESS TO MEDICINES

3.1 Background

3.1.1 Definitions of innovation in legislation

A review of national legislation and policy documents of the 48 countries in the WHO European Region covered by the PPRI networks, supported by a recently published paper (22), found few references to definitions of pharmaceutical innovation. It also found that definitions varied between the countries.

Some countries (including Austria, Belgium, Bulgaria, Poland, Serbia and the United Kingdom) use the term innovation in legislation because the concept (or degree) of innovation usually plays a role in decisions about whether a medicine should be included in public funding, and under which conditions. The degree of innovation is usually expressed in terms of the (added) therapeutic value; societal considerations may also be considered (as in the United Kingdom – see section 3.3.1). New on-patent, first-in-class medicines that are the first to treat a specific illness (or address an as-yet unmet medical need) tend to be considered innovative; they are thus likely to be included in public funding at higher prices. The concept of innovation may not necessarily be defined or operationalized, however – even when innovation is mentioned as a necessary assessment criterion for reimbursement (as in Spain) (22). Examples from legislative texts that use the concept of innovation are provided in Annex 1.

3.1.2 Overview of identified policies

The literature review’s mapping exercise identified 12 existing types of pricing, procurement and/or reimbursement policies to support innovation and access that have been implemented in at least one of the 48 countries studied. Two are assessment tools to generate evidence on the degree of innovation, with a view to informing evidence-based decision-making. Ten further policies can be categorized as innovation incentives – designed as either exemption or deviation from the standard system or process – and as policies to support access to innovation. Collaborative approaches, which may be intra-country or cross-country, supplement the national policies identified. Fig. 1 shows the categories of instruments and policies applied to innovation and access to medicines identified and included in the study.
3.2 Supporting preparedness of systems and early launch of innovation

3.2.1 Horizon scanning systems

Horizon scanning is defined as “systematic identification of health technologies that are new, emerging or becoming obsolete and that have the potential to effect health, health services and/or society” (25). An emerging health technology in this context is one that has not yet been adopted within the health-care system (for example, a medicine in phase II or III clinical trials or at pre-launch stage, or a medical device in the pre-marketing stage).

Horizon scanning systems have not been introduced widely in the Region. Of the 48 countries reviewed, five (Italy, the Netherlands, Norway, Sweden and the United Kingdom) apply horizon scanning systematically – at least for some new medicines – and five others perform some horizon scanning activities (such as Austria for oncology medicines). In total, 38 countries have no horizon scanning system yet, but Albania and Belgium reported plans to introduce one (Table 1). The scope and design of horizon scanning also differs – for instance, in terms of the timing of the scanning (how early before marketing authorization it aims to detect possible new medicines) (36).

Horizon scanning has gained importance in recent years – in particular, since a case in 2014, when planned market entry of a high-priced medicine to treat hepatitis C took policy-makers...
Table 1. Status of horizon scanning systems, by country

<table>
<thead>
<tr>
<th>Horizon scanning status</th>
<th>Countries</th>
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<tbody>
<tr>
<td>Systematic use of horizon scanning for some new medicines</td>
<td>Italy, Netherlands, Norway, Sweden, United Kingdom</td>
</tr>
<tr>
<td>Some horizon scanning/forecasting activities</td>
<td>Austria, Denmark, France, Ireland, Malta</td>
</tr>
<tr>
<td>No horizon scanning, but plans to introduce it</td>
<td>Albania, Belgium</td>
</tr>
<tr>
<td>No horizon scanning</td>
<td>Armenia, Azerbaijan, Belarus, Bulgaria, Croatia, Cyprus, Czechia, Estonia, Finland, Georgia, Germany, Greece, Hungary, Iceland, Israel, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Luxembourg, North Macedonia, Poland, Portugal, Republic of Moldova, Romania, Russian Federation, Serbia, Slovakia, Slovenia, Spain, Switzerland, Tajikistan, Türkiye, Turkmenistan, Ukraine, Uzbekistan</td>
</tr>
</tbody>
</table>

* Systematic use of horizon scanning for some medicines in the inpatient sector only and some horizon scanning activities in the outpatient sector.

Sources: Information routinely collected from PPRI network members; (10,11,15,36).

by surprise (37). Alerts of medicines in the pipeline, including potentially innovative products and those with high price tags, allow policy-makers to make prioritization decisions (such as ensuring availability of funds for innovation) at early stages. Horizon scanning helps policy-makers to identify possible candidates for HTA processes (as in Norway – see section 3.3.1) and to start collecting evidence of medicines even before their marketing authorization, as these data are needed later for pricing and reimbursement decisions.

Establishment of a horizon scanning system is resource-intensive and costly, however (36). To address this challenge, countries may decide to work together. The most prominent example in this context is the International Horizon Scanning Initiative (IHSI) launched by the Beneluxa Initiative (Box 1).

### 3.2.2 Early access schemes

Several countries have early access schemes in place to ensure access to medicines that are not yet authorized. One variant is for compassionate use, as provided for by European Union (EU) legislation (Article 83 of Regulation (EC) No. 726/2004 (41)). This allows use of a medicine without marketing authorization under strict conditions for defined patient groups who have no satisfactory authorized therapy for their disease and cannot enter clinical trials.

Medicines that address an unmet medical need and/or that are considered a priority from a public health perspective are typical candidates for early access schemes. These schemes grant access to medicines before pricing and reimbursement decision-making has started, and prices paid by the public payer are usually not regulated through standard policies. The price of a medicine under an early access scheme is usually determined before an HTA is undertaken, and thus on a somewhat weak basis (Box 2).
Box 1. IHSI

IHSI was initiated by the Beneluxa Initiative on Pharmaceutical Policy, which is a cross-national collaboration of five European countries: Austria, Belgium, Ireland, Luxembourg and the Netherlands (38). Beneluxa member countries work together in defined areas, such as HTA and joint negotiations.

IHSI is a spin-off, since countries that are not involved in the Beneluxa Initiative can also join. In October 2019, IHSI was established as an independent legal entity (39). As of August 2021, IHSI has eight member countries: Belgium, Denmark, Ireland, the Netherlands, Norway, Portugal, Sweden and Switzerland.

In early 2020, a tender was launched with the aim of selecting a provider to build and implement a joint IHSI horizon scanning database. The task comprises two elements: the technical infrastructure to host the database, and a scientific component relating to data collection, which is intended to populate the database continuously. A contract was awarded in June 2021, and IHSI is expected to deliver results in 2022 (40).

Box 2. Early access schemes in France and the United Kingdom

**Autorisation temporaire d’utilisation (ATU) [Temporary Authorization for Use] in France**

The ATU system is the French early access scheme and comprises medicines intended to treat serious or rare diseases in the absence of appropriate treatment, and when treatment cannot be postponed. Medication costs are covered by the social insurance fund. Physicians can request a normative ATU for individual patients, or the pharmaceutical company can apply for a cohort ATU for a patient group (42,43).

Free pricing applies under the ATU, which means that the pharmaceutical company can set the price. Once the medicine has received marketing authorization, a price negotiation usually takes place between the government’s interministerial Pricing Committee and the company; this is informed by an HTA. If the negotiated price is lower than the ATU price, the pharmaceutical company has to pay back the difference.

**Early Access to Medicines Scheme in the United Kingdom**

The United Kingdom launched the Early Access to Medicines Scheme (EAMS) in 2014. This aims to provide access to medicines for life-threatening or seriously debilitating conditions that do not yet have marketing authorization when there is a clear unmet medical need. Under the scheme, companies can apply to the Medicines and Healthcare Products Regulatory Agency for a promising innovative medicine designation and request an EAMS opinion on the risks and benefits of the medicine, based on data gathered from the patients who will benefit from it. Medicines under the EAMS are provided to patients on the National Health Service (NHS) in the United Kingdom (44,45).
Early access schemes offer an opportunity for faster access to innovation, but they are procedures outside the standard processes and frequently offer incentives and exemptions. Allowing free pricing by the pharmaceutical company can result in a higher price than that set under price regulation. Clarity on the criteria used to designate which medicines are eligible for an early access scheme – and for how long – can help to move the medicine into the standard policy framework after a defined period and/or on loss of eligibility.

3.3 Value assessment

Value assessment relates to approaches in which determination of the price of a medicine funded by a public payer is guided by its therapeutic and economic value. This is of particular importance for potentially innovative medicines, since they are defined by the (therapeutic) value they offer to patients and the health system. For medicines and health technologies, advances have been made to develop a sound and established methodology for value assessment (HTA), and policies have been implemented that consider the value as determined by an HTA.

3.3.1 HTA

HTA is “a multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle. The purpose is to inform decision-making in order to promote an equitable, efficient, and high-quality health system” (46). Assessed dimensions can include clinical effectiveness; safety, costs and economic implications; ethical, social, cultural and legal issues; and organizational and environmental aspects, as well as wider implications for the patient, relatives, caregivers and the wider population. The overall value may vary depending on the perspective taken, the stakeholders involved and the decision context.

Several countries have introduced HTA, and 37 of the 48 countries reviewed use HTA or HTA components to inform their pricing and reimbursement processes. Only 12 countries use HTA systematically, however (Table 2).

Across these countries, HTA systems vary in terms of their scope, methods and processes. They also differ in the institutional role of the system and its links to pricing and reimbursement. Some countries (such as France, Germany, Ireland, Poland and the United Kingdom) have created designated independent HTA bodies that conduct the assessments; these outcomes are then used by pricing and reimbursement agencies in their negotiations. Such structures facilitate systematic and frequent use of HTA in pricing and reimbursement decision-making, but they are resource-intensive. In other countries (including Austria, Finland, Italy, Latvia, Portugal and the Republic of Moldova), HTA is performed by experts within the institution that also determines or negotiates the (reimbursement) price – usually the social health insurance fund or an NHS unit (14,15,47,48).

HTA can take many forms, which vary in the scope of evidence assessed and, consequently, in the extent of information they offer and the resources they require. A decision on the type of HTA that is most suitable – as well as whether to conduct an HTA at all – can be determined by evidence generated at an earlier stage, such as through horizon scanning (Box 3).
Table 2. Systematic use of HTA for pricing and/or reimbursement decisions, by country

<table>
<thead>
<tr>
<th>Use of HTA</th>
<th>Countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systematic HTA use in pharmaceutical pricing and reimbursement</td>
<td>Denmark, Germany, Hungary, Latvia, Lithuania, Malta, Netherlands, Norway, Poland, Portugal, Sweden, United Kingdom</td>
</tr>
<tr>
<td>Use of HTA components in the pricing and reimbursement process</td>
<td>Austria, Belgium, Bulgaria, Croatia, Czechia, Estonia, Finland, France, Greece, Iceland, Ireland, Israel, Italy, Kazakhstan, Luxembourg, Republic of Moldova, Romania, Russian Federation, Serbia, Slovakia, Slovenia, Spain, Switzerland, Türkiye, Ukraine</td>
</tr>
<tr>
<td>No use of HTA, but plan to introduce it</td>
<td>Cyprus, North Macedonia</td>
</tr>
<tr>
<td>No use of HTA</td>
<td>Albania, Armenia, Azerbaijan, Belarus, Georgia, Kyrgyzstan, Tajikistan, Turkmenistan, Uzbekistan</td>
</tr>
</tbody>
</table>

Sources: Information routinely collected from PPRI network members (14,15,47,48).

An HTA can be used as a form of gatekeeping. In the Netherlands, for instance, all medicines with an expected high-budget impact have to undergo an HTA before any further decision is made (Box 4).

The design of the HTA methodology used has implications. For example, the methodology applied in England, United Kingdom, provides for consideration of two additional criteria, through which the HTA body is guided to provide a positive recommendation even if the standard cost–effectiveness threshold is exceeded (Box 5).

Box 3. Nye Metoder [New Methods] for the managed introduction of new health technologies in Norway

In 2013, Nye Metoder was introduced as the National System for Managed Introduction of New Health Technologies within the Specialist Health Service in Norway (49,50). The aim was to provide a consistent process for assessment and decision-making on public funding for all new health technologies – including medicines – in the inpatient setting.

Three different types of HTA are used systematically for all new health technologies: mini-HTAs are limited assessments conducted by clinicians and supporting units in hospitals; single technology assessments against one comparator are performed by the Norwegian Medicines Agency; and full HTAs against several comparator technologies are undertaken by the Norwegian Institute of Public Health. A committee with federal and regional representatives (payers) decides on the type of HTA to be performed. This decision is informed by a horizon scanning notification, which is prepared – in the case of medicines – by the Norwegian Medicines Agency, assisted by a literature review provided by the Norwegian Institute of Public Health. The outcomes of the horizon scanning exercise are publicly accessible in a database managed by the Norwegian Institute of Public Health. Since the beginning of 2018, the findings of horizon scanning on outpatient medicines may also lead to performance of an HTA.
Box 4. Obligatory HTA for expensive hospital medicines in the Netherlands

The Dutch Healthcare Institute performs an HTA for each medicine that is to be included in the outpatient reimbursement list, but this mechanism was not previously used for the hospital sector. As a result, medicines with high prices had fast uptake in hospitals, despite a lack of evidence.

This practice was stopped in 2014, with the introduction of the lock policy. Since then, if a medicine for the inpatient sector has either an estimated total budget impact of more than €40 million for all patients or an estimated annual cost of €50 000 per patient plus a total cost of more than €10 million per patient over a period of three years, it is blocked from automatic reimbursement. Instead, it must undergo a full HTA, which determines the follow-up processes. These include a decision for or against coverage, and potential price negotiations – including implementation of an MEA – by the Ministry of Health (47,51,52).

Box 5. Higher cost–effectiveness thresholds for end-of-life medicines and highly specialized technologies in England, United Kingdom

The United Kingdom National Institute for Health and Care Excellence (NICE) – the English HTA body – provides assessments and appraisals of health technologies to ensure uptake of cost-effective innovation in health care. If NICE recommends a health technology, the NHS is obliged to make funding available.

NICE assesses the incremental cost–effectiveness of a technology by calculating the incremental cost–effectiveness ratio (ICER), which expresses the monetary cost of each additional quality-adjusted life-year (QALY) of the technology in comparison to alternative interventions currently in use. Health technologies are usually recommended for funding by NICE with an ICER of £20 000 based solely on cost–effectiveness considerations.

Technologies with an ICER between £20 000 and £30 000 can also be considered for funding, but further factors need to be considered, comprising both additional health benefits and non-health objectives, such as costs and benefits incurred outside the NHS. These include needs of disabled people, relief of stigma and distribution of benefits to the most disadvantaged groups to reduce health inequalities. In addition, the innovative nature of a technology is an important aspect to consider – specifically, whether the innovation would add demonstrable and distinctive benefits that are substantial and may not have been fully captured in the calculation of a technology’s cost–effectiveness.

Positive recommendations by NICE above the £30 000 threshold are possible in two cases. First, the end-of-life criterion allows appraisal committees to give greater weight to QALYs offered by life-extending technologies indicated for patients with a short life expectancy. Such technologies are indicated for patients with a life expectancy of less than 24 months, and they should extend life by at least three months, compared with current NHS treatment. Second, medicines for ultra-rare conditions are appraised using highly specialized technology assessments, for which the ICER threshold can be increased to £300 000 (23,53–61).
HTA is of major importance to manage the entry of a new medicine into a health system by generating and assessing evidence to determine the (added) value of the medicine, as far as existing evidence allows. Final decisions on funding a medicine and its price lie with the policy-makers, however. As the following sections show, a decision to fund a medicine assessed as not cost-effective can be made if doing so aligns with societal values or other policy objectives (such as industry goals).

### 3.3.2 Value-based pricing (VBP)

VBP – through which authorities set the price and decide on the funding of a medicine based on an assessment of its value – has been positioned as an important policy to support innovation and access, but it lacks a clear or agreed definition. Broadly speaking, consideration of value (typically added therapeutic value, as determined in an HTA) in pricing and reimbursement decisions is a value-based approach, or a policy based on value components (62). A fully-fledged VBP, however, includes the consideration of value alongside other criteria (such as costs for manufacturing or R&D and forecasted patient groups) in pricing and reimbursement. It relates to a framework in which the pricing and reimbursement decision is an integrated process, fully and exclusively based on an assessment of the value of the medicine. Sweden is the only country with a fully-fledged VBP system (Box 6). England, United Kingdom, also intended to move to a full VBP scheme in 2014, but implementation was discontinued (63).

**Box 6. VBP in Sweden**

In 2002, Sweden introduced a fully-fledged VBP system, in which pricing and reimbursement processes are completely integrated. Medical assessors, health economists and legal counsellors at the Dental and Pharmaceutical Benefits Agency review the clinical evidence and health-economic documentation provided by pharmaceutical companies that apply for a price and inclusion in the reimbursement system. This system is, in principle, product oriented, so decisions on reimbursement status are made per product (for all indications, for a limited area of indications or only for a specified patient group).

Eligibility for reimbursement is assessed against three criteria: the human value principle to guard against discrimination (in terms of sex or age, for example); the need and solidarity principle that gives priority to those in greatest need (thus, people with more severe diseases are prioritized over people with less severe conditions); and the cost–effectiveness principle. Cost–effectiveness is analysed from a societal perspective, and all relevant costs and revenues for treatment and ill health are considered, regardless of who (the state, county council, municipality or patient) pays or benefits. The cost of using a medicine should be reasonable from a medical, humanitarian and socioeconomic perspective.

Reimbursement and pricing processes are performed simultaneously, and result in a joint decision. The board rejects applications for reimbursement if the price is too high and the medicine does not fulfil the decision criteria. The company may then decide whether to apply again at a different price. The reimbursement decision depends on several factors, including the negotiation of an MEA between the county councils (the payers) and the pharmaceutical company (64–67).
While consideration and appraisal of evidence inform pricing and reimbursement decisions on potentially innovative medicines, the concern remains that use of value assessments as the sole basis for such decisions means that further important components – for example, need, prevalence and affordability – are disregarded as being distinct from value (68). WHO recommends VBP if certain conditions are met, including its implementation in conjunction with other pricing policies; availability of adequate resources and skilled personnel; inclusion of an analysis of the budget impact and affordability from the payer’s and patient’s perspectives in the HTA; transparent processes; and explicit methods and perspectives for determining value (69).

3.4 MEAs

To support the inclusion of potentially innovative medicines with high price tags in public funding (reimbursement) of national health systems, public payers in several countries have implemented MEAs. An MEA is defined as “an arrangement between a manufacturer and payer/provider that enables access to (coverage/reimbursement of) a health technology subject to specified conditions. These arrangements can use a variety of mechanisms to address uncertainty about the performance of technologies or to manage the adoption of technologies in order to maximize their effective use, or limit their budget impact” (70).

MEAs are typically classified as financial MEAs (including simple discounts, capping and price–volume agreements) and performance-based (or outcome-based) MEAs (such as coverage with evidence, risk-sharing and pay-for-performance schemes) (71). For the latter, patient health outcomes after some time of treatment affect the price (discount) and whether the medicine remains in public funding.

At least 31 countries are known to have implemented MEAs for some new medicines. Most (but not all) countries that do not apply MEAs are those with no or limited medicine price regulation (Table 3).

Overall, the number of countries that have implemented MEAs has grown in the last decade, although the number of MEAs per country varies. While financial MEAs tend to be more common, increasing use of performance-based MEAs has been observed. These are particularly used to ensure access to pharmaceutical innovation, including more complex therapies, where there is uncertainty over the additional clinical benefit at launch due to an immature evidence base. Major areas in which MEAs have been implemented are therapeutic areas in which pharmaceutical innovation is needed: oncology, rheumatology, hepatitis C and orphan medicines (74,75,77).

Confidentiality is a major feature of all types of MEA. In some countries, it is not even known which medicines are subject to an MEA, or which types of MEA are in use (74,77). The discounted aspect is, as a rule, confidential in all countries, meaning that there is no way for payers to assess whether the discount granted was higher or the same as in other countries. Theoretically, given their confidential character, MEAs would incentivize pharmaceutical companies to propose higher list prices (to factor in the price reductions that will be granted in confidential deals), and this was confirmed empirically by one study (80). Suzanne Hill, former Director of the Essential Medicines and Health Products
MEAs are intended to serve two purposes: to allow access to new high-priced medicines that would otherwise not be affordable and to manage uncertainty in the face of limited evidence on clinical outcomes. The MEA policy option is one of four pricing and reimbursement policies discussed in the OMI technical report by Docteur (18), including their possible impacts on affordable access to effective new medicines. Docteur concludes that it is not clear whether MEAs and related agreements will play a significant role in helping to attain more affordable and timely access to care.

Overall, a major discrepancy exists between government expectations of this policy and the dearth of evidence about its impact. Despite increased use of MEAs, few evaluations have been undertaken. This may be linked to the confidentiality around important parts of these agreements (for instance, an evaluation of MEA in Belgium had to be discontinued (77)). To the author’s knowledge, only one study (conducted in Italy a decade ago) is available that suggests an MEA led to faster access to medicines (81).

Performance-based MEAs, which are increasingly being used, could play an important role in evidence generation as they collect real-world data. They could thus help to specify the degree of innovativeness of a medicine under an MEA and to identify additional innovation needed (as the current medicine under the MEA cannot, as anticipated, address the medical need). Real-world data are not always collected or analysed appropriately, however, in part because of the significant administrative efforts and expertise required. According to a Dutch study, which analysed MEAs from 2006 to 2012, for a third of the research questions defined at the start date, the evidence generated through outcome research studies was insufficient to draw robust conclusions four years later (82).
3.5 Free pricing

Free pricing relates to a situation in which governments allow pharmaceutical companies to determine the price of the medicine they launch (25). It is the opposite of price regulation, through which pricing policies – defined as a set of written principles or requirements for managing the prices of medicines, agreed or adopted by a public institution (such as a government), a group of purchasers or individual health services – are implemented. Pharmaceutical pricing policies are set up to “explicitly focus on achieving affordable and equitable access to quality-assured pharmaceutical products for consumers and health systems, which should ensure value-for-money based on improved health outcomes at the population level, as well as maintaining supply security of high-quality products” (69).

Not all countries have yet implemented price regulation – for example, there is free pricing for the majority of medicines (except those which are procured) in several central Asian countries (16). In other countries in the Region – including most EU member states – free pricing is usually allowed for non-prescription medicines and non-reimbursed medicines (that is, those not covered by the public payer) (15). Medicines considered innovative are usually subject to price regulation because this allows policy-makers to achieve intended policy objectives, such as sustainability, access or innovation.

A lack of pricing policies is usually the result of limited capacity to create them. In a few cases, however, free pricing is deliberately used as a policy to support innovation and access. Pharmaceutical companies may set the price of a medicine at their own discretion, and this price is covered by the public payer. This approach is applied in Germany, where in the first 12 months after market entry of a medicine the public payer funds the price set by the company. If the negotiated price based on an HTA conducted during that year is lower, no payback is required from the company (see section 4.2 for further details). In this policy environment, new medicines come on the market quickly, since the company can launch them as soon as a marketing authorization has been granted. (In other countries, decisions on price and inclusion in reimbursement are made first.) Free pricing in Germany aims to support and accelerate access to (potentially) effective innovative medicines. It comes at a cost, however, since there is a trade-off with affordability and sustainability for the health system.

3.6 Additional funding

Three policies that offer additional funding for pharmaceutical companies, beyond what the standard system of policies would normally grant, were identified to have been implemented in some countries.
3.6.1 Innovation funds

Specific funds (sometimes called innovation funds) offer a privileged pathway for defined medicines (such as innovative medicines and medicines to address unmet medical need) to ensure their (early) access and uptake.

These dedicated funds offer extra money (for example, from the federal government) and thus support public payers (such as the regions and health insurers) whose budget would not normally cover paying for expensive innovative medicines. In some cases, the eligibility criteria for these funds differ from those that are usually applied. As a result, specific funds may provide public coverage for medicines that do not meet the requirements of a standard HTA. An example of such a fund is the Cancer Drugs Fund (CDF) in England, United Kingdom. At its inception, the CDF financed cancer medicines that NICE had assessed as not cost-effective (Box 7).

Cancer medicines are typical candidates for innovation funds, as are orphan medicines. The review also identified a number of specific funds in other countries (Table 4).

Empirical evidence on these funds – mainly based on the experience with the initial version of the CDF – points to some limitations and risks. First, it is not clear whether these funds actually support access to innovation or whether they provide access to medicines that are not cost-effective and forego the proof of evidence (83,85). When no evaluation is undertaken, or when the HTA is waived, pharmaceutical companies may be incentivized to charge higher prices (100). In some countries these funds were introduced

Box 7. CDF and the Innovative Medicines Fund in England

England, United Kingdom, introduced the CDF in October 2010. Its purpose was to fund cancer medicines that the NHS would normally not cover after the HTA body NICE had assessed them as not cost-effective (or if an HTA had not yet been performed). The CDF soon experienced overspending on its initial budget, with funding of more than £200 million in 2013–2014.

The CDF had originally been implemented as a temporary measure until implementation of a planned VBP system in 2014. When the VBP scheme was abandoned, however, the CDF was prolonged and reformed in 2016. It was changed into a managed access mechanism to fund oncology medicines for a maximum period of two years to enable data to be collected to resolve uncertainty. During this time, the medicines had to undergo an HTA performed by NICE. This change was implemented in response to fierce criticism of the practice that funded medicines had previously not had to provide any proof of value (83–89).

In July 2021, establishment of the Innovative Medicines Fund was announced to ensure early patient access to potentially life-saving new treatments (for example, in the areas of spinal muscular atrophy and cystic fibrosis). This Fund builds on the existing and continuing CDF, and will operate in the same way: while funding is provided from the NHS, data are collected and an HTA is conducted by NICE during the period. The new Fund has an additional budget of £340 million (90).
Table 4. Innovation funds identified, by country

<table>
<thead>
<tr>
<th>Country</th>
<th>Fund name</th>
<th>Medicines included</th>
<th>Further information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belgium</td>
<td>Special Solidarity Fund</td>
<td>Orphan medicines (those that have not yet received a positive reimbursement recommendation and meet at least one of the following criteria: treatment of a rare disease requiring a specific physiopathological treatment, treatment of a rare disease requiring a continuous and complex treatment, treatment of chronically ill children, involvement of innovative treatment techniques or otherwise requiring medical treatment abroad)</td>
<td>The Special Solidarity Fund is considered to serve as a safety net that offers temporary funding. Patients submit an application for reimbursement individually after they have exhausted all other public or private reimbursement options at the national, European or international levels (91–93).</td>
</tr>
<tr>
<td>Croatia</td>
<td>Especially Expensive Medicines Fund</td>
<td>Typically, biologicals for the treatment of cancer, autoimmune and rare diseases, including cancer medicines, orphan medicines and some other expensive medicines (mainly hospital medicines)</td>
<td>The Especially Expensive Medicines Fund has a separate budget, and MEAs are frequently implemented for medicines on this list. Separate approval is needed from the Croatian Health Insurance Fund (94–96).</td>
</tr>
<tr>
<td>England, United Kingdom</td>
<td>Cancer Drugs Fund</td>
<td>Cancer medicines (in the beginning): those not considered cost-effective</td>
<td>See Box 7 for details.</td>
</tr>
<tr>
<td>England, United Kingdom</td>
<td>Innovative Medicines Fund</td>
<td>Potentially life-saving therapies (such as for spinal muscular atrophy and cystic fibrosis)</td>
<td>See Box 7 for details.</td>
</tr>
<tr>
<td>Italy</td>
<td>Fondi Innovativi [Innovation Fund]</td>
<td>One fund for innovative oncology medicines and one for innovative non-oncology medicines, each worth €500 million; merged into a single fund from 2022</td>
<td>Assessment criteria for eligibility are unmet medical need, added therapeutic value and robustness of evidence. The funds offer separate financing for eligible medicines for 36 months. Eligible medicines also enjoy further benefits, including exemptions from discounts and paybacks and direct access to the market (97,98).</td>
</tr>
<tr>
<td>Poland</td>
<td>Not known</td>
<td>Innovative medicines without equivalents and those in ultra-orphan indications (99)</td>
<td>No further details are known.</td>
</tr>
</tbody>
</table>

as a temporary measure but developed into long-term solutions that required regular increases in funding. Concerns have also been raised about the “budget silo mentality” (101) of these separate funds, as they constitute a parallel world to standard pricing and reimbursement processes that are based on careful selection and decisions guided by evidence. Use of the innovation funds instrument can require decision-making with a lack of evidence, which may weaken the steering control of policy-makers (12). Given the risks of funding through separate budgets, at a minimum, mitigation measures should be put in place to ensure that clear eligibility criteria are defined and that regular monitoring and evaluation are conducted.
3.6.2 Diagnosis-related group carve-outs

If medicines are used in public hospitals, they are usually funded through diagnosis-related groups (DRGs) – a funding scheme applied to hospitals in many countries (102). Through DRG funding, hospitals are remunerated for defined services (procedures), regardless of how much money they actually spend.

Medicines are part of the DRG funding system; as such, they are not reimbursed on a case-by-case basis, as they are in the outpatient sector. Any mechanism through which hospitals receive individual remuneration for medicines supports purchase and uptake of medicines. This policy option of a non-priced related incentive also concerns separate budgets (or funds or positive lists); it is thus a variant of innovation funds (32,103) (see section 3.6.1).

DRG carve-outs are exemptions from standard DRG funding; they ensure that hospitals receive separate product-specific funding for eligible medicines, while bundled remuneration through DRG continues to be applied for the remaining medicines (104). While DRG funding is the common financing scheme for hospitals in Europe, DRG carve-outs are rare (Table 5).

Overall, DRG carve-outs are frequently designed for cancer medicines and/or orphan medicines, as these are expensive. In France, high price tags of the medicines are even a criterion to be included in the additional list. DRG carve-outs are also considered a policy option to encourage hospital use of novel antibiotics that create lower risk of AMR, since these medicines are funded separately, whereas bundled DRG funding incentivizes use of less expensive antibiotics (12,104).

Countries that apply these tools consider them accelerators for pharmaceutical innovation (107,108). Timing is a major issue, as DRG carve-outs help to ensure separate funding early after marketing authorization; this is seen as a temporary measure to encourage early innovation. In France, however, while medicines in principle lose their eligibility for the Liste en sus after some time, they are not moved back to the standard system. This ties up money that could be used elsewhere. Defining clear eligibility criteria and monitoring whether medicines still comply with the defined prerequisites is critical to using these incentives.

3.6.3 Exemptions from payments to public payers

Another financial incentive is a waiver of payments (or reduction in payments) that pharmaceutical companies are normally requested to transfer to public payers for defined medicines. Such payments may be requested for all new medicines (as statutory mandatory discounts) or in cases of spending that exceeds defined ceilings. Exemptions from or reductions in these payments for public payers are mainly granted for orphan medicines (Table 6).
### Table 5. Additional lists (budgets) for DRG carve-outs, by country

<table>
<thead>
<tr>
<th>Country</th>
<th>Fund name</th>
<th>Medicines included</th>
<th>Further information available</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>Single Medical Procedures</td>
<td>Oncology medicines only</td>
<td>Inclusion in the Single Medical Procedures list can be requested once a year (105, 106).</td>
</tr>
<tr>
<td>France</td>
<td>Liste en sus [additional list]</td>
<td>Expensive medicines that meet the following criteria: mainly used in hospitals, important therapeutic benefit, added therapeutic benefit, price too high to be covered through the DRG system</td>
<td>As soon as the criteria are no longer met, the medicines are supposed to be removed from the list (although in practice, this is not the case – e.g., a biosimilar comes onto the market, but the biological originator stays in the list at the high price) (42, 104).</td>
</tr>
<tr>
<td>France</td>
<td>Liste des médicaments de rétrocession [list of reassigned medicines]</td>
<td>Medicines with limitations in supply, dispensing or administration, or which require prescription and delivery monitoring; including medicines derived from blood, antiviral medicines, chronic hepatitis B or C medicines, antibiotics, antifungals, orphan medicines and cancer medicines</td>
<td>This is less an instrument to encourage access and uptake of innovation like the Liste en sus; rather, it is designed more to manage supply limitations (medicines on this list can also be dispensed in community pharmacies) (42).</td>
</tr>
<tr>
<td>Germany</td>
<td>Neue Untersuchungs- und Behandlungsmethoden (NUB) [New diagnostic and treatment methods] list</td>
<td>New technologies, including new medicines</td>
<td>Hospitals can request inclusion of these medicines in the NUB list – valid for one year – to accelerate innovation in hospitals via separate tariffs for medicines that are applicable soon after launch, as consideration of new medicines in updated DRG calculations would take too long (107).</td>
</tr>
</tbody>
</table>

Notes: In addition, the Especially Expensive Medicines Fund in Croatia, which mainly concerns medicines used in hospitals, could also be included in this policy option (96). This list is not exhaustive: further DRG carve-outs may be applied in other countries.

### 3.7 Procurement mechanisms to support innovation and access to medicines

Procurement is a process to purchase goods and services (in this case, medicines); it involves several steps and stakeholders, based on national or supranational regulation, policies, structures and procedures (25). The WHO Regional Office for Europe encourages Member States to conduct more strategic procurement of medicines (114). This requires consideration of various value criteria instead of solely price as the award criterion, and more collaborative approaches (115). Procurement has been shown to drive prices down through competition between suppliers; this contributes to affordability, at least
Table 6. Exemptions from or reductions in payments to public payers, by country

<table>
<thead>
<tr>
<th>Country</th>
<th>Statutory payments to public payers</th>
<th>Privileged medicines benefiting from waiver or reduction</th>
<th>Financial supporting mechanisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>A claw-back (called a safeguard clause), through which a pharmaceutical company has to pay financial contributions to the social health insurance fund when public expenditure exceeds a stipulated threshold (defined by the net turnover of the pharmaceutical company)</td>
<td>Orphan medicines and generics</td>
<td>Exemption from the claw-back (until 2019) (42,104)</td>
</tr>
<tr>
<td>Italy</td>
<td>A statutory discount(^a) for pharmaceutical company payments to public payers, amounting to a cumulative discount of 9.75% (the so-called &quot;5% + 5% discount&quot;) of the price for any new medicine in the first year</td>
<td>Medicines assessed as fully innovative (based on the criteria of unmet medical need, added therapeutic benefit and high evidence proof – the last not applicable for orphan medicines)</td>
<td>Exemption from the statutory discount (109–112)</td>
</tr>
<tr>
<td></td>
<td>Paybacks to public payers if national thresholds for pharmaceutical expenditure are exceeded</td>
<td>Orphan medicines and medicines assessed as fully innovative (criteria listed above)</td>
<td>Exemption from the payback</td>
</tr>
<tr>
<td>Spain</td>
<td>A statutory discount(^a) of 7.5% of the medicine price (discounts to be shared between manufacturers, wholesalers and pharmacists)</td>
<td>Orphan medicines</td>
<td>Reduced statutory discount (4%) (113)</td>
</tr>
</tbody>
</table>

Notes: This list is not exhaustive; further exemptions or reductions may be applied in other countries.

\(^a\) Statutory discounts are published in legislation and apply to all pharmaceutical companies, in contrast to commercial discounts negotiated between the payer and the company on an individual – usually confidential – level.

in the short term, but may risk availability (for example, via shortages, low participation rates of bidders in tender calls or withdrawals of suppliers from markets for commercial reasons) and – eventually – access. Strategic procurement is intended to mitigate these shortcomings and support access and – ideally – innovation. The following sections present two country procurement policies that have the potential to support innovation and access.

3.7.1 Pooled procurement

Pooled (or joint) procurement requires collaboration among (public) purchasers, who increase their purchasing power by pooling their volumes (as well as pooling expertise, knowledge and resources) (116). In this scenario, one purchaser utilizes demand from multiple users (such as hospitals). This is a particularly important approach for purchasers who represent smaller volumes or markets, and/or who operate in resource-restrained settings (such as poorer regions). It is thus a measure to support access.

Pooled procurement has a number of variants, and can be applied within or across countries. As an intra-country policy, pooled procurement can be conducted through group procurement by hospitals or hospital groups, regional procurement or centralized procurement at the national level (as in Denmark, Norway and Portugal; Box 8). For further information on cross-country procurement, see section 3.8 and the OMI technical report by Docteur (18).
Box 8. Centralized procurement for hospital medicines in Denmark, Norway and Portugal

Mandatory central procurement for Danish public hospitals

The Danish central procurement agency, Amgros, was founded in 1990, with the aim of procuring nearly all medicines and medical devices used in public hospitals. It is owned by the Danish regions, which are also the owners of the hospitals, and now has over 100 staff. Hospitals have to use Amgros for procurement.

Amgros applies a lifecycle approach to secure hospital needs, resulting in use of different procurement practices for different medicines, including price negotiation for new medicines and tendering for medicines with competition. It engages in communication with users (hospitals) and suppliers, and considers knowledge of the market and dialogue the key prerequisites for successful procurement.

Amgros has been able to generate important savings, but some challenges remain – such as securing availability of “old” established medicines with low prices – since Denmark is a relatively small market and thus insufficiently attractive to pharmaceutical companies. To address this challenge, Amgros has engaged in cross-country joint procurement projects (117–123).

Voluntary central procurement for Norwegian public hospitals

Norwegian public hospitals are also owned by the regions, which established and own a procurement agency for the inpatient sector. In contrast to Denmark, centralized procurement in Norway was introduced as a bottom-up initiative. In 1995, after only six months of preparation, the then Legemiddelin NKjøpsamarbeidet (LIS) [Drug Procurement Cooperation] was founded, with the backing of national authorities and regional leaders. It was renamed Helseforetakene Inntkjøpservice AS (HINAS) [Health Trusts’ Purchasing Service] and integrated into the general hospital procurement agency in 2016. Political support in the starting phase, when centralization of purchasing was met with opposition, is considered a reason for its successful development.

LIS/HINAS organizes tenders for nearly all medicines funded by hospitals. While there is no obligation for hospitals to engage in centralized purchasing, they mainly use LIS/HINAS to secure lower prices. Hospitals are incentivized to procure economically, since funding of some medicines for outpatient use (such as medicines for treatment of tumour necrosis factor, multiple sclerosis and hepatitis B and C) has been transferred from the social insurance fund to hospital budgets.

From the beginning, LIS/HINAS has involved doctors extensively in preparation of tenders. Based on clinical guidance of experts from hospitals, it makes recommendations for products, which usually correspond to the lowest-priced medicines. LIS/HINAS organizes regular seminars in hospitals to inform doctors and pharmacists of the results of the tenders. As in Denmark, Norwegian procurement experts consider exchanges with and involvement of various stakeholders (including users in hospitals) an important prerequisite, since it ensures acceptance and use of centralized procurement. This is particularly important in Norway, as centralized procurement is voluntary (123–125).
There is evidence that pooled procurement (within a country and across countries) has contributed to lower prices (affordability), to delivery of medicines not otherwise supplied (access) and to enhanced governance and transparency, all of which are principles of the OMI (31,115,123,127). National centralized procurement may still not be sufficient to ensure access to new and potentially innovative medicines, however: even aggregated volumes at the national level may be too low to make the market attractive for suppliers. This was highlighted by some central procurement bodies – in particular from smaller markets – and was a major motivation for joining forces across countries and collaborating in cross-country procurement projects such as the joint Nordic tenders in the Nordic Pharmaceutical Forum and pooled vaccines purchases by the Baltic Procurement Initiative (128) (see section 3.8).

3.7.2 Subscription fee-based procurement models

A relatively new policy option is a subscription fee-based procurement model (also called the Netflix® or the all you can eat model, sometimes also referred to as the all you can treat model). This is another pull mechanism to incentivize R&D (see Moon et al. (19)) and access to innovation.

One-well known instance of this model is its implementation for hepatitis C medicines in Australia. In 2016, the Australian government concluded a five-year contract with five manufacturers for unlimited use of hepatitis C medicines. In return, the manufacturers were granted a fixed sum (1 billion Australian dollars) for the period March 2016 to February 2021. The aim was to provide predictable revenue for pharmaceutical companies while also being able to offer treatment to all patients who needed it (129,130). In 2019, Louisiana in the United States also signed a subscription fee-based model for hepatitis C medicines (131).
Use of this model has also been considered for (novel) antibiotics (132): purchasers would pay a pre-agreed amount to use as much or as little of the medicines as they needed, in contrast to the normal business model for companies to optimize profit through volume increases. England, United Kingdom, and Sweden are piloting this procurement model for new antibiotics (Box 9), but it is too early to draw conclusions yet.

3.8 Policies to encourage uptake of biosimilar medicines

Biosimilar medicines (medicines developed to be similar to existing biological medicines – the reference medicines) are considered promising solutions to ensure affordable access to biological medicines after patent expiry. Biosimilar (and generic) medicines build on the pharmaceutical innovation of the originator; they are critical to promoting competition,

**Box 9. New procurement models for novel antibiotics piloted in England, United Kingdom, and Sweden**

In 2019, the government announced a commercial model for antibiotics for England, United Kingdom, in which pharmaceutical companies are paid a fixed annual fee upfront for an unlimited supply. The subscription fee, which was reported to be up to £10 million per product, is determined based on an HTA performed by NICE. As the standard HTA does not take into account the particularities of novel antibiotics, a new cost–effectiveness evaluation methodology specific to new antibiotics is being developed.

By the end of 2020, after a rigorous process with expert clinical input, the first two medicines (cefiderocol and ceftazidime with avibactam) were selected for assessment, which was planned to be conducted within 12 months. The antibiotics are expected to be made available to patients via a subscription fee-based payment model from early 2022.

Sweden has piloted a similar subscription fee-based model for novel antibiotics since 2018. Again, suppliers are granted a fixed annual revenue; the model particularly aims to address low-volume antibiotics, which might be unattractive for suppliers.

In early 2020, the Swedish Public Health Agency launched a call for an open tender procedure and invited pharmaceutical companies to submit candidate medicines for the pilot. These candidate medicines should be antibiotics with efficacy against a pathogen included in the Priority 1: Critical group of the WHO priority pathogens list (133) and with an acceptable safety profile. Two-year contracts with five suppliers of antibiotics were implemented in June 2020. A fixed guaranteed annual revenue was set for each antibiotic. This was calculated based on the cost of a security stock, at a price 30% higher than the average of European list prices.

In procuring antibiotics under this pilot, hospitals continue to purchase as normal, and pay the difference between the guaranteed annual revenue and actual sales. In cases of unexpectedly large volumes that would lead to the guaranteed annual revenue being exceeded, a bonus would be paid by the hospitals to the pharmaceutical companies (104,134–138).
increasing spending efficiency and contributing to access to innovation at affordable prices on patent expiry (69) (see also Docteur (18), which discusses possible pricing and reimbursement policies). In addition, promotion of the competition of off-patent medicines (including generic and biosimilar medicines) is also seen as a policy option to support innovation and access (20), as it frees up funds to be used for innovation. As many reference biologicals are considered innovative at the time they are marketed, launch and use of biosimilars years later provide access to these innovations but at affordable prices (lower prices of biosimilar medicines and also of the biological reference medicines, which may have decreased in price due to competition).

A number of pricing and reimbursement policy measures can be implemented for off-patent medicines. Importantly, these need to be supplemented by demand-side measures targeted at doctors, pharmacists and patients to ensure that they all trust these medicines and prescribe, dispense or consume them.

Several countries allow or advise doctors to prescribe biosimilar medicines for treatment-naive patients and to switch from the reference medicine to a biosimilar, or from a biosimilar to another biosimilar medicine; this is usually linked to defined conditions such as shared decision-making with patients and close monitoring (139). Few countries allow pharmacists to dispense a biosimilar instead of a prescribed biological reference medicine or another prescribed biosimilar (so-called biosimilar substitution), however (140). In contrast, substitution at the pharmacy level (dispensing a generic instead of the prescribed originator medicine or another generic) has commonly been implemented for chemical molecules. Generic substitution is in place in 43 of the 47 countries in the WHO European Region for which information is available, whereas only 12 countries also allow substitution of biosimilars (Table 7). This reflects differences of opinion among experts and policymakers on the substitutability of biological medicines.

Table 7. Generic and biosimilar substitution, by country

<table>
<thead>
<tr>
<th>Generic or biosimilar substitution</th>
<th>Countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generic substitution and biosimilar substitution allowed</td>
<td>Belarus, Cyprus, Czechia, Estonia, Iceland, Israel, Latvia, Malta, Norway, Poland, Russian Federation, Türkiye</td>
</tr>
<tr>
<td>Generic substitution allowed; biosimilar substitution to be introduced</td>
<td>Germany</td>
</tr>
<tr>
<td>Generic substitution allowed; biosimilar substitution not allowed</td>
<td>Albania, Belgium, Croatia, Denmark, Finland, France, Greece, Hungary, Ireland, Italy, Kazakhstan, Kyrgyzstan, Lithuania, North Macedonia, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland, Ukraine</td>
</tr>
<tr>
<td>Generic substitution allowed; no information on biosimilar substitution</td>
<td>Armenia, Azerbaijan, Georgia, Republic of Moldova, Serbia, Tajikistan, Turkmenistan, Uzbekistan</td>
</tr>
<tr>
<td>Neither generic substitution nor biosimilar substitution allowed</td>
<td>Austria, Bulgaria, Luxembourg, United Kingdom</td>
</tr>
</tbody>
</table>

Note: No data available for Turkmenistan.
Sources: Information routinely collected from PPRI network members (14,15,139).
Caution or even reluctance among some actors towards use of biosimilars may also be attributable to their relative novelty (the first marketing authorization of a biosimilar in the EU was granted in 2006) compared to generics, which have been marketed for decades. Many countries have had long-term experience with demand-side measures to enhance the uptake of generics. Lessons learned from policies for generic medicines can inform implementation of biosimilar policies. One key message is that action is needed to establish acceptance of any off-patent (generic and biosimilar) medicines by patients, prescribers and pharmacists – for example, through education programmes.

3.9 Collaborative approaches

The potential of policy options to reach intended objectives can be reinforced by collaborative approaches (see also Docteur (18) and Moon et al. (19)), which mainly consider the impact of pooling on incentivizing research and development). Collaboration in pharmaceutical policies may take different forms, depending on the countries and policy areas or topics concerned. For instance, the collaboration might be organized at a local, regional or national level, or it might be cross-country (for example, European or global). The collaboration might also address one specific policy area or dimension in the pharmaceutical value chain (horizontal collaboration), or comprise several policies represented by different stakeholders across the value chain, and thus constitute vertical collaboration.

Fig. 2 shows examples of different topic-related or cross-topic (vertical) collaborations within or across countries in the WHO European Region. Further details of these collaborations are provided in Annex 2.

**Fig. 2. Dimensions of collaboration in pharmaceutical policies**

FINOSE: HTA collaboration between Finland, Norway and Sweden; IHIS: International Horizon Scanning Initiative.
The potential of collaborative approaches (independent of their dimension) lies in their pooling of expertise, knowledge and resources, as well as their contribution to reducing duplication of activities (redundancies). Some policies with strong potential to support innovation and access are resource-intensive (such as horizon scanning); it is therefore difficult for an individual country to undertake them alone. Vertical collaboration among authorities across the pharmaceutical value chain – reflecting a holistic approach – can be beneficial, as it can contribute to improved mutual understanding among those involved of the challenges and possible solutions. For instance, it may help all stakeholders to understand that the data needs of downstream actors – such as HTA bodies and payers – are different from those of regulatory authorities who decide on marketing authorization.

Collaborative approaches may offer several benefits, but their implementation may be challenging – in particular in the case of cross-country collaborations, given potential legal, institutional and organizational differences. Prerequisites for successful collaboration include sufficient resources for all those involved in the collaboration; trust and mutual understanding of the partners; commitment; an overall strategy and political backing; a functional working structure; and, depending on the activities of the collaboration, stakeholder management (see also the roadmap for establishing successful cross-country collaboration (141)).
The two case studies on Italy and Germany presented below showcase how a toolbox of country innovation policies can be designed. Italy was chosen because it implemented a bundle of policy measures to encourage innovation, including innovation funds, frequent use of MEAs and several early access schemes. Germany aims to encourage early access by allowing immediate market entry after marketing authorization at a price that the pharmaceutical company sets and the public payer funds. The German case study also includes information on policies to foster market entry of novel antibiotics to address AMR.

The case studies offer a brief overview of the policies identified. Section 4.3 analyses which of the innovation policies presented in the section 3 findings are implemented in Italy and Germany. For Italy, a more detailed description is available as web-annex on the WHO Regional Office for Europe website.

4.1 Case study on policies to support access and innovation in Italy

Health care in Italy is organized as an NHS, based on three levels: central government; 21 regional governments, which fund the health services – including medicines – in their territories; and local health authorities, which are in charge of health-care provision in the outpatient and inpatient sectors in their areas (111). The Agenzia Italiana del Farmaco (AIFA) [Italian Medicines Agency] at the central level is mandated with several responsibilities, including marketing authorization, pharmacovigilance, pricing and reimbursement, and measures to support rational use. Pricing and reimbursement decisions are made following AIFA’s negotiations with the pharmaceutical company.

In 2017, Italy introduced two innovation funds to allow additional funding beyond the standard reimbursement system for eligible medicines (those assessed as innovative). Linked to this policy, a new definition of innovation was developed and operationalized. The innovation status of a medicine is measured in terms of its compliance with three criteria: unmet medical need, added therapeutic benefit and quality of evidence. Based on an assessment conducted through the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology, a medicine is considered to be fully innovative (in the case of orphan medicines, this rating is even possible if the quality of evidence is low), conditionally innovative or not innovative (142,143).

Fully and conditionally innovative medicines are granted immediate access to regional reimbursement lists without any regional or local reassessment. Fully innovative medicines are eligible to access the innovation funds from which they will be financed for 36 months. Until the end of 2021, each of the innovation funds – one for innovative oncology medicines and one for innovative non-oncology medicines – was worth €500 million. After the 36 months of additional funding, the regions have to pay for the medicines as usual (97).
From 2022, one fund for all innovative medicines equipped with a total of €1 billion is in place, resulting from a merger of the two funds (144).

Fully innovative medicines also enjoy additional benefits. In Italy, pharmaceutical companies normally have to pay back to the public payers if defined national pharmaceutical expenditure ceilings are exceeded; fully innovative medicines are exempt from this payback mechanism. Fully innovative medicines are also exempt from a legally stipulated mandatory manufacturer discount granted to AIFA for a period of the first 36 months (97,143,145).

AIFA has implemented numerous MEAs with pharmaceutical companies to ensure innovation and access to new medicines with possibly low evidence. MEAs in Italy are managed either at the patient level via registers (financial MEAs, such as cost-sharing and capping, and performance-based MEAs, such as payment by results, risk-sharing and a success fee) or at the population level (financial arrangements such as budget caps and price–volume agreements). Recently, Italy introduced a new variant of performance-based MEAs: payment at results, through which the payer only disburses payment on achievement of a specific milestone. This MEA was used to fund Chimeric antigen receptor T cell therapies (146).

Italy applies various mechanisms to facilitate early access to medicines that have not yet received a marketing authorization (for an overview of all early access schemes, see the long version of the case study in web-annex or the summary in section 4.3). One early access scheme concerns public funding from the National AIFA Fund for the use of non-authorized orphan medicines and other medicines for the treatment of serious diseases (147). This is also called the 5% fund because it is fed by 5% of annual promotional expenses of pharmaceutical companies (148). This 5% fund also serves to finance independent pharmaceutical research (149).

To encourage pharmaceutical innovation, Italian legislation also facilitates accelerated access through fast-track pricing and reimbursement procedures for orphan medicines, medicines of special therapeutic and social relevance, and hospital medicines (110). While Italy has several policies to encourage pharmaceutical innovation, it aims to balance the objectives of access to innovation and sustainability. The latter is also addressed by AIFA’s activities on ensuring responsible use of medicines (including prescribing guidelines and monitoring of prescribing and consumption) and benefiting from therapeutic equivalence (such as encouraging uptake of generic and biosimilar medicines).

4.2 Case study on policies to support innovation and access and to fight AMR in Germany

The German health system is based on a multipayer social health insurance system, with strong competitive elements between the payers (sickness funds) (150). Responsibilities are divided between the federal government; federal states (“Länder”), which are responsible
for service provision; and self-governing bodies with specific tasks. These include the Gemeinsamer Bundesausschuss (G-BA) [Federal Joint Committee], which determines the added therapeutic value of a medicine based on an HTA and, thus, defines the pathway for reimbursement, and the National Association of Statutory Health Insurance Funds, which negotiates with the company on the reimbursement price.

The German pharmaceutical policy framework is legally defined by the Arzneimittelmarkt-neuordnungsgesetz [Act on the Reform of the Market for Medicines (AMNOG)], which aims to support pharmaceutical innovation and early access to medicines. As soon as a medicine has received marketing authorization, it may be launched on the German market, and it is automatically eligible for reimbursement for the first 12 months (unless it is in the negative list of medicines excluded from reimbursement). The pharmaceutical company may set the price at its own discretion (free pricing at market entry), and this will be reimbursed for 12 months.

During the first six months, the HTA body – the Institute for Quality and Efficiency in Healthcare – is commissioned by G-BA to conduct an HTA, called an early benefit assessment, to determine the added benefit of the medicine. In principle, no HTA is performed for orphan medicines, as their added benefit is taken as a given, unless their annual social health insurance expenditure is expected to exceed €50 million.

Based on the added benefit determined by G-BA, the National Association of Statutory Health Insurance Funds negotiates with the company the reimbursement price that will be valid from month 13. No payback mechanisms are in place, even when the negotiated reimbursement price is below the price originally set by the pharmaceutical company for the first year (151). The plan of the new German government is to reduce this period to six months.

If no additional benefit is determined, G-BA assesses whether the medicine can be clustered into a reference price group of comparable medicines. The reimbursement price for medicines included in the German reference pricing system is equal for all medicines in that group; the difference between the reference price and the higher pharmacy retail price has to be borne by the patient out of pocket.

Since 2018, AMNOG is also applicable for medicines exclusively used in hospitals, so these medicines are also subject to an HTA (152). As in many other countries, medicines used in German hospitals are funded through the DRG system – a bundled financing mechanism for services in hospitals (see section 3.6.2). Hospitals may request additional funding beyond the DRG financing for new technologies, including new medicines (DRG carve-outs). To be eligible for such additional funding, the medicine must be included in the NUB list.

The standard innovation pricing, procurement and reimbursement policies implemented in Germany also apply to novel antibiotics (for initiatives to encourage research and development of novel antibiotics, see Moon et al. (19)). For instance, early launch of (novel) antibiotics is supported by the opportunity to market the medicine immediately on authorization, automatic reimbursement eligibility and free pricing for the first year, as well as accessibility of additional NUB funding.
In addition, the German system offers specific incentives for last-resort antibiotics. In line with the Law on Fair Competition of Sickness Funds in the Statutory Social Health Insurance, an antibiotic is considered a last-resort (or reserve) antibiotic if it is effective against infections caused by multidrug-resistant bacterial pathogens for which only limited alternative therapy options are available. By the end of 2020, the Robert Koch Institute had to determine, in consultation with the Federal Institute for Drugs and Medical Devices, the criteria for classifying an antibiotic as last-resort. An inexhaustive list of 21 multidrug-resistant bacterial pathogens and criteria was published in February 2021 (153).

Medicines classified as last-resort antibiotics are exempt from HTA; as with orphan medicines, their added therapeutic value is assumed without need for proof of evidence (154). Furthermore, since 2017, last-resort antibiotics can benefit from not being clustered in the reference pricing system (optional), as their contribution to AMR can be taken into consideration (104).

4.3 Summary of application of identified innovation policies in the case study countries

Table 8 provides an overview of identified policies to support innovation and access to medicines (including novel antibiotics) in Italy and Germany. As with this technical report in general, this summary is focused on policies for authorized medicines, including specific schemes to use and include medicines that are not yet authorized in the health system. Incentives to encourage research and development for medicines of unmet medical need, such as novel antibiotics, is not within the scope of this paper; alternative business models for promoting R&D, including emerging approaches, are presented in another OMI technical report (19).

While the pharmaceutical policy framework differs, there are some similarities between the case-study countries. Both Italy and Germany have several policies to encourage pharmaceutical innovation, for which they are willing to pay (for example, by offering financial incentives through higher prices, or through no or lower discounts to be granted by companies). Both also focus on robust evidence to be considered in the HTA assessment (in Italy, this aspect was strengthened recently, with new criteria for the pricing and reimbursement process and for the assessment rules for pharmaceutical innovation). Early access is an objective in both countries, and both seem willing to trade robustness of evidence for earlier access to medicines considered of particular relevance. The focus on pharmaceutical innovation is supplemented by several efforts to foster competition in the off-patent market to generate efficiency gains, and to use these savings to fund innovation in both countries. Finally, both have experienced regular reforms and changes, with the aim of optimizing the pharmaceutical policy framework.
Table 8. Overview of policies to support innovation and access and their use in Italy and Germany

<table>
<thead>
<tr>
<th>Policy</th>
<th>Italy</th>
<th>Germany</th>
</tr>
</thead>
<tbody>
<tr>
<td>Country policies</td>
<td>A horizon scanning project was initiated by the Veneto region, with reports 36, 18 and 12 months before marketing authorization – this has been discontinued at the national level. AIFA has conducted some horizon scanning initiatives (36).</td>
<td>No systematic horizon scanning is done.</td>
</tr>
<tr>
<td>Horizon scanning</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early access schemes</td>
<td>Various early access schemes for non-authorized medicines are in place, including:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• off-label use of non-authorized medicines with full public funding;</td>
<td>Compassionate use programmes are in place (156).</td>
</tr>
<tr>
<td></td>
<td>• compassionate use under certain conditions (medicine to be supplied free of charge);</td>
<td>The German reimbursement system is designed to encourage early access: as soon as a medicine has a marketing authorization, it can be launched in the German market and will be reimbursed for the first 12 months at a price set by the company (157).</td>
</tr>
<tr>
<td></td>
<td>• financing of non-authorized medicines for serious diseases from the National AIFA Fund (5% fund), fed by pharmaceutical companies based on the extent of promotional expenses;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• non-repetitive use of non-authorized medicines for advanced therapies in urgency and emergency situations (111,143,147,149).</td>
<td></td>
</tr>
<tr>
<td>HTA</td>
<td>HTA is conducted by internal services of AIFA as the basis for pricing and reimbursement decisions. A 2021 decree put a stronger focus on added therapeutic value (111).</td>
<td>The HTA system is well developed, transparent and based on robust evidence. HTA is conducted by the Institute for Quality and Efficiency in Healthcare (150).</td>
</tr>
<tr>
<td>VBP</td>
<td>Pricing and reimbursement decisions made by AIFA are based on negotiations with the company and strongly based on value-based elements (although no fully integrated VBP is in place) (111).</td>
<td>No VBP system per se is in place, but HTA outcomes play an integral role in pricing and reimbursement decisions (156).</td>
</tr>
<tr>
<td>Policy</td>
<td>Italy</td>
<td>Germany</td>
</tr>
<tr>
<td>------------------------</td>
<td>----------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>MEAs</td>
<td>MEAs are used frequently, at both the patient level via registers (financial and performance-based MEAs) and the population level (financial MEAs) <em>(111,146)</em>.</td>
<td>No MEAs are used at the national level in pricing and reimbursement decisions. However, in follow-up negotiations between hospitals or sickness funds and payers, an MEA can be implemented.</td>
</tr>
<tr>
<td>Additional funding</td>
<td>Two innovation funds of €500 million each offer separate funding for innovative oncology medicines and innovative non-oncology medicines for 36 months. In 2022, these were merged into one fund of €1 billion <em>(97,143–146)</em>.</td>
<td>Data not available</td>
</tr>
<tr>
<td>DRG carve-outs</td>
<td>Data not available</td>
<td>Add-on NUB funding is available for defined technologies, including medicines on request. For medicines used in hospitals the standard funding is the bundled funding through DRGs. Specific NUB funding can also be requested to encourage purchase and use of novel – and thus more expensive – medicines in hospitals to combat AMR <em>(107)</em>.</td>
</tr>
</tbody>
</table>
| Further financial incentives | Medicines assessed to be fully innovative are exempt from:  
• the mandatory manufacturer discount granted to AIFA;  
• paybacks applicable in cases of exceeding national pharmaceutical expenditure ceilings *(97,143,145)*. | No payback mechanism is in place, even when the negotiated reimbursement price (valid from the second year) is below the freely set price of the manufacturer in the first year (which is publicly funded) *(151)*. Exemptions from mandatory manufacturer discount are available for some products. |
<p>| Pooled procurement     | Pooled procurement takes place in some of the regions (via centralized regional procurement). For some medicines (mainly generics), support from the national procurement agency is given to provision of framework agreements (such as for biosimilar medicines) and contracts based on the dynamic purchasing system: a public procurement technique, similar to a framework agreement, but allowing possible bidder to join the system on an ongoing basis. | No centralized procurement is done, but several group procurement schemes are in place in the hospital sector.                                                                                               |
| Subscription fee-based models | Data not available                                                  | Data not available                                                                                                                                                                                    |</p>
<table>
<thead>
<tr>
<th>Policy</th>
<th>Italy</th>
<th>Germany</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policies to encourage uptake of biosimilars</td>
<td>In principle, the focus is on exploiting competition and using efficiency gains of therapeutically equivalent medicines (generics and biosimilar medicines) to foster competition. Simpler and faster procedures for therapeutically equivalent medicines (since October 2020) and prescribing by international non-prescribing name are allowed. Generic substitution is allowed, but not biosimilar substitution. In the case of three or more biosimilar medicines of an active substance being marketed, a multi-award agreement must be concluded in procurement (111).</td>
<td>Several policies to promote the uptake of biosimilar medicines are in place since August 2022: introduction of biosimilar substitution at the community pharmacy level planned for August 2022 (139).</td>
</tr>
<tr>
<td>Cross-country activities</td>
<td>Cross-country collaboration Italy is one of the founding members of the cross-country collaboration, the Valletta Declaration, which aims to collaborate on horizon scanning, HTA and joint negotiations (141).</td>
<td>Data not available</td>
</tr>
</tbody>
</table>
The aim of this technical report was to identify pricing, procurement and reimbursement policies to support innovation and access to medicines applied in the WHO European Region, and to describe countries’ experience with them. The policies presented are not blue sky ideas: they have been implemented (or piloted) in at least one country in the Region, and thus offer some proof of concept.

Some of the policies described – particularly innovation incentives – come at a cost, since high prices, increased revenues and further financial incentives for pharmaceutical companies are among common triggers to encourage innovation. Nevertheless, further price and non-price related mechanisms for incentivizing innovation also exist (15,32). Countries need to be aware of possible trade-offs between encouraging pharmaceutical innovation and reward investment and other policy objectives, including affordable and equitable access. Innovation policies – particularly those offering (financial) incentives and awards to companies – may risk falling short of the access principle and may compromise sustainability, which is another core principle of the OMI. Prioritization in favour of (funding) innovative medicines for only a few patients may substantially limit financial resources for other medicines, such as high-volume medicines for chronic diseases.

Among the 12 country policies identified to support innovation and access to medicines, some options require higher trade-offs and are more challenging with regard to the objectives defined as pillars of the OMI. These are mainly the innovation incentives, which are deviations from standard procedures, exemptions or additional funding. This paper has also identified instruments to help mitigate some of the risks of these innovation incentives, however. These comprise assessment tools, such as HTA, which should be integrated as good practice in any decisions made by authorities on the pricing and funding of new medicines.

Benefits of HTA and evaluations have been proven. HTA supports policy-makers by providing a transparent and reproducible assessment of evidence and offering a framework for its appraisal. It provides information on the extent of (added) therapeutic value and the degree of innovation, since initially promising therapies may result in limited innovation. HTA is resource-intensive, however, so its implementation can be difficult for lower-income countries (158), which have to give priority to establishing a publicly funded benefit package of essential medicines. To address this challenge, countries may decide to reuse HTA reports from other countries and adapt them to their national context, and to benefit from cooperation (through voluntary cross-country collaborations or those coordinated at a supranational level).

Horizon scanning, another assessment tool identified, is an important prioritization instrument as it aids in the selection of medicine candidates that could be followed up
with an HTA. As with HTA, horizon scanning is very useful, but depending on its scope and implementation approach, it can require considerable capacity and resources. Again, collaboration (to pool resources) may be an avenue for countries interested in this activity.

While policy-makers benefit from horizon scanning and HTA to generate evidence on which to base their decisions, a lack of clarity of concepts may undermine the potential of these generally useful tools. Despite political interest to support innovation, many countries have not defined this concept. Operationalization of key concepts helps technical experts in public authorities to prepare decisions on pricing and reimbursement; in addition, this would enhance transparency and help to orient all stakeholders involved. Clear and transparent concepts may also help authorities with communicating negative funding decisions to the public – for example, by demonstrating that the medicine did not meet defined criteria.

Innovation incentives may compromise sustainability and solidarity due to privileged treatment of some therapies (and thus diseases and patient groups). In many countries in the Region, MEAs are a frequently used policy option to ensure access to potentially innovative medicines. As discussed in the OMI technical report on shared responsibility in pharmaceutical pricing, coverage and reimbursement (18), there is a trade-off between early access at high cost and high risk versus delayed access at reduced cost. In addition, the frequent use of confidentiality clauses limits sharing of price information. An opportunity to develop MEAs towards greater – but not full – price transparency is to negotiate clauses to share actual prices with public authorities (such as procurement bodies) in the same country, or to develop a system of anonymous sharing (a clearing house mechanism) that reduces opacity while not compromising contractual obligations (159). Another contribution to improved transparency and evidence generation is collection of real-world data following a conditional pricing and reimbursement decision, as this facilitates reducing uncertainty and reviewing the decision at a later stage, when more data are available.

For MEAs and other innovation incentives that require trade-offs (such as free pricing), attaching conditionalities can steer incentives and awards to compliance with certain principles. Such conditionalities may include provision of information on the share of public funding in R&D of a specific medicine or negative outcomes of clinical trials by the pharmaceutical company with the public authority.

Another risk of innovation incentives is that some are designed as exemptions to standard processes (such as funding from other sources, lower evidence requirements and limited transparency). If these policies cannot be embedded in the routine system, clear criteria are necessary to specify the eligibility of medicines for exemptions and incentives.

The OMI aims to find solutions to ensure better access to effective, novel, high-priced medicines, based on the pillars of solidarity, transparency and sustainability. Some innovation policies – in particular incentives – do not always comply with these principles but, as described above, approaches exist to mitigate the risks (such as collection of evidence, clarity of concepts, assessments and prioritization processes, and sharing of
data with authorities). Some policies to support innovation and access do not require trade-offs between objectives, however, as in the case of policies that make use of HTA (VBP), of competition (policies to enhance the uptake of biosimilar medicines) and of collaborative approaches (pooled procurement), or that pilot new avenues outside the common business model rationale (such as subscription fee-based procurement, which does not require higher volumes for increasing profits of companies). Some of these policies are new, and more experience must be gained to bolster the evidence on their application.

For all policies (independent of whether they focus more on incentivizing innovation or ensuring access, including affordability and sustainability), monitoring and evaluation is necessary, and adaptation after some time may be useful to align them to new environments and to consider lessons learned from implemented policies. In addition, when introducing or adjusting policies, reflections can be made on the design of a policy in a more collaborative way (for example, via institutionalized dialogue with stakeholders, consideration of experiences and evidence – such as HTA – from other countries, and assessing or procuring jointly with similar institutions), since collaborative approaches between authorities alongside the pharmaceutical value chain in a country and across countries have been proven to contribute to access to novel medicines.
References


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ANNEXES
## Annex 1.
### Definitions of innovation in national legislation

Table A1.1 shows examples of how innovation is defined in legislative texts in some countries in the WHO European Region.

### Table A1.1. Definitions of innovation in legislative texts

<table>
<thead>
<tr>
<th>Country</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>The extent of therapeutic benefit for patients or of significant therapeutic innovation is based on pharmacological, medical-therapeutic and health-economic documents submitted by the company applying for inclusion in reimbursement. The company is obliged to indicate when the patent protection of the active ingredients contained in the respective medicines will end in Austria (1). The following eight criteria are used to determine the degree of innovation of the medicine being applied for (in order of increasing degree of innovation).</td>
</tr>
<tr>
<td></td>
<td>1. The medicine applied for has the same active ingredient, the same active ingredient strength and the same or practically the same dosage form as one or more medicines already listed in the reimbursement code (follower product with the same active ingredients).</td>
</tr>
<tr>
<td></td>
<td>2. The medicine applied for has the same active ingredient, the same or practically the same dosage form as one or more medicines already listed in the reimbursement code, but a new active ingredient strength.</td>
</tr>
<tr>
<td></td>
<td>3. The medicine applied for has a new combination of active ingredients that are already listed in the reimbursement code.</td>
</tr>
<tr>
<td></td>
<td>4. The medicine applied for is a new form of administration of an active ingredient listed in the reimbursement code or an active ingredient combination listed in the reimbursement code.</td>
</tr>
<tr>
<td></td>
<td>5. The medicine applied for has a new active ingredient from an active ingredient group listed in the reimbursement code with a uniformly defined active principle.</td>
</tr>
<tr>
<td></td>
<td>6. The medicine applied for has a new active ingredient with a new active principle for the treatment of a disease for whose treatment specialty medicines are already listed in the reimbursement code.</td>
</tr>
<tr>
<td></td>
<td>7. With the medicine, it is possible for the first time to treat a disease with medication that was previously not treated with medication.</td>
</tr>
<tr>
<td></td>
<td>8. For the first time, treatment of an illness is possible with the medicine applied for (2).</td>
</tr>
</tbody>
</table>
Table A1.1. Contd.

<table>
<thead>
<tr>
<th>Country</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belgium</td>
<td>There are three categories of therapeutic value (classes 1, 2 and 3). Products within Class 1 are considered new innovative medicines. To be labelled as Class 1, medicines must have an added therapeutic value compared to other medicines. Orphan medicines are also included in Class 1 if they meet additional criteria (Law of 14 July 1994 on compulsory health care and compensation insurance) (3).</td>
</tr>
</tbody>
</table>
| Bulgaria | Council Decree 81 of 2003 stipulates the criteria, conditions and procedures for including medical products in the Bulgarian positive list. Three groups of medicines to be included in the positive list have been defined, the first two of which are innovative products:  
  - new medicines without a medicinal alternative in the clinical practice (new mechanism of action, new Anatomical Therapeutic Chemical code);  
  - new medicines for which there is a therapeutic alternative with pharmacotherapeutic advantages;  
  - medicines with a medicinal alternative in the clinical practice (generics) (4). |
| France | Medicines are considered innovative if they demonstrate a rate of improvement in medical value of I to III (on a scale of I to V). These include:  
  - new therapeutic area, reduction of mortality (level I);  
  - significant improvement in efficacy and/or reduction of side-effects (level II);  
  - modest improvement in efficacy and/or reduction of side-effects (level III).  
Based on the Social Security Code, the medical value is based on an assessment of efficacy and tolerance, the position of a medicine within the therapeutic area, the preventive, curative or symptomatic activity and public health interest, and the added therapeutic value (5,6). |
| Italy | According to Determinazione 1535/2017 [Decision 1535/2017], three criteria define the innovativeness of a medicine:  
  1. Unmet medical need;  
  2. Added therapeutic benefit;  
  3. Quality of evidence (robustness of clinical studies), as assessed through GRADE methodology.  
There is no formal link between the innovation evaluation and the price and reimbursement negotiations (7). |
| Kazakhstan | Innovative medical technologies are defined as methods and means of scientific and technical activities which are socially significant and/or cost-effective when implemented in the field of medicine (biomedicine), pharmacy and digitalization of health care (8). |
| Poland | The principles the Polish HTA agency followed to create the first list of medical technologies with a high level of innovation are as follows (9):  
  - Medicines for which a decision on marketing authorization in the centralized EU procedure was issued from 1 January 2020 to 26 November 2020 were assessed.  
  - Medicines for which the decision granting marketing authorization in the central procedure in the EU covers the use in oncology or in rare diseases were assessed. |
The Polish HTA agency then assesses the products in terms of:

- characteristics of the evaluated medicine technology;
- unmet health need;
- expected health effects and strength of the intervention;
- economic impact on the budget of the public payer.

Source: Correspondence between the author and the Ministry of Health of Poland, 29 March 2021.

Spain

Legislation sets out a medicine’s degree of innovation as one of the criteria which determines whether it will be publicly funded (alongside criteria such as severity of the disease; the therapeutic and social value of the medicine; and incremental clinical benefit considering its cost–effectiveness or budget impact).

However, despite the degree of innovation being listed in legislation and formally required for reimbursement decisions, no published definition of the concept is available; nor is there a commonly accepted methodology to measure it (10).

United Kingdom

Innovation as it relates to medicines is referenced in multiple documents. The *Guide to the methods of technology appraisal, fourth edition* of June 2008, *Social value judgements: principles for the development of NICE guidance, second edition* of July 2008 and *Guide to the methods of technology appraisal, fifth edition* of April 2013 state that the innovative nature of a technology will be considered in its appraisal and determination of whether it is an effective use of NHS resources. This involves consideration of whether the innovation adds demonstrable, distinct, significant and substantial benefits which may not have been adequately captured in the measurement of health gain during the assessment.

In cases where the technology’s health-related benefits may not have been included in the quality adjusted life-year calculation of its impact, then the *Single technology appraisal: user guide for company evidence submission template* of January 2015 requires companies to “state whether and how the technology is a ‘step-change’ in the management of the condition [and] provide a rationale to support innovation, identifying and presenting the data you have used” (11).

Annex 1. References


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1 All references accessed 1–2 May 2022.

Cross-country collaboration has been observed particularly in the areas of marketing authorization, HTA and procurement. In EU member states and associated countries in the European Economic Area, marketing authorization has been harmonized since 1995, with an EU-wide procedure of a single application, a single evaluation and a single authorization for most new medicines. A similar harmonization for the marketing authorization of medicines became mandatory for the member countries of the Eurasian Economic Union at the beginning of 2021 (1).

Over the last decade, collaboration in HTA has been strengthened across European countries, and the European Network for Health Technology Assessment initiative has been an important contributor to this process (2). The Network has made major advances in development of methodologies in HTA, with the aim of reducing redundancies and duplication of efforts among the countries involved. Initially a European Commission-supported project begun in 2007, it was prolonged twice and eventually comprised 81 organizations (HTA agencies, public authorities for pricing and reimbursement, and research institutes) from 29 European countries.

In January 2018, the European Commission published a proposal on future collaboration in HTA in Europe, which included provisions for use of HTA methods and procedures across the EU. The proposal addressed joint clinical assessment as well as joint scientific consultations (early dialogue) and identification of emerging health technologies (horizon scanning) (3). In June 2021, an agreement was reached between the European Parliament and the European Council on enhanced collaboration in this area, so that EU member states will use joint clinical assessment reports conducted at the EU level in their national or regional HTA processes and complement these with their assessments of non-clinical HTA dimensions (economic, social and ethical aspects) (4). In addition, various cross-country collaborations led by national governments also work together jointly on HTA, such as the Nordic collaboration, FINOSE, and the Beneluxa Initiative (further details provided below).

Until recently, collaboration between European countries on pharmaceutical pricing and reimbursement has been somewhat informal. It included, for instance, sharing of experiences with different pricing and reimbursement policies in networks of competent authorities such as the PPRI network (5) (with a specific regional PPRI EECA network for countries in eastern Europe and central Asia) and the Piperska group (6), and at meetings organized by the WHO Reginal Office for Europe or the European Commission for the Network of Competent Authorities for Pricing and Reimbursement (7). A higher level of
formalization was implemented with the establishment of the European Integrated Price Information Database (EURIPID), which was initiated in 2010 as a voluntary non-profit collaboration of national pricing and reimbursement authorities in European countries to share list prices of reimbursable medicines (8). Confidential prices are not shared, however, although EURIPID was requested to provide such by the European Parliament (9).

Some discussion has taken place on possibly aligning pricing and reimbursement policies across European countries. The European Commission, for instance, commissioned a study to explore possibilities, feasibility and a potential design for differential pricing among EU member states (10), but this concept has not been followed up.

To move forward with collaboration, some European countries decided to collaborate formally in the areas of pricing and procurement, HTA and reimbursement – these cross-country collaborations are called voluntary collaborations to emphasize that they are coordinated by national governments and not by European or international organizations. Table A2.1 provides an overview of some of these collaborations in the WHO European Region.

Table A2.1. Voluntary cross-country collaborations in pharmaceutical policies

<table>
<thead>
<tr>
<th>Collaboration</th>
<th>Start date</th>
<th>Countries involved (2021)</th>
<th>Scope of health technologies</th>
<th>Scope of collaboration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baltic Procurement Initiative</td>
<td>2021</td>
<td>Estonia, Latvia, Lithuania</td>
<td>Medicines and vaccines; medical devices (only for lending)</td>
<td>Procurement Lending (in cases of lack of availability)</td>
</tr>
<tr>
<td>Beneluxa Initiative</td>
<td>2015</td>
<td>Austria, Belgium, Ireland, Luxembourg, Netherlands</td>
<td>Medicines (focus on new high-priced medicines)</td>
<td>Horizon scanning HTA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pricing and reimbursement negotiations</td>
<td></td>
</tr>
<tr>
<td>FAAP</td>
<td>2017</td>
<td>Croatia, Czechia, Hungary, Lithuania, Poland, Slovakia; Latvia (as an invited guest)</td>
<td>Medicines (focus on new high-priced medicines)</td>
<td>HTA Pricing and reimbursement negotiations</td>
</tr>
<tr>
<td>FINOSE</td>
<td>2018</td>
<td>Finland, Norway, Sweden</td>
<td>Medicines (focus on new medicines)</td>
<td>HTA</td>
</tr>
<tr>
<td>Nordic Pharmaceutical Forum</td>
<td>2015</td>
<td>Denmark, Iceland, Norway, Sweden; Finland (as an observer)</td>
<td>Medicines (focus on new high-priced and “old” low-priced medicines)</td>
<td>Horizon scanning Procurement</td>
</tr>
<tr>
<td>Valletta Declaration</td>
<td>2017</td>
<td>Croatia, Cyprus, Greece, Italy, Malta, Portugal, Romania, Slovenia, Spain</td>
<td>Medicines (focus on new high-priced medicines)</td>
<td>Horizon scanning HTA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pricing and reimbursement negotiations</td>
<td></td>
</tr>
</tbody>
</table>

FAAP: Fair and Affordable Pricing; FINOSE: HTA collaboration between Finland, Norway and Sweden; HTA: health technology assessment.

Sources: Vogler et al. (11), Dental and Pharmaceutical Benefits Agency (12).
In addition to information sharing, these collaborations aim to work on concrete joint procurement projects – including joint pricing and reimbursement negotiations – HTA and horizon scanning (see also the IHSI spin-off from the Beneluxa Initiative presented in Box 1). All were established relatively recently, and some of their activities are in preparation or at a pilot phase. Nevertheless, some results have been produced. The Baltic Procurement Initiative successfully jointly procured three vaccines (after one failed procurement project); the Nordic Pharmaceutical Forum successfully concluded the first Nordic procurement project and launched a call for a second joint tender in 2021; and two countries in the Beneluxa Initiative successful concluded a joint reimbursement negotiation after a failed one (13).

In some of the cross-country collaborations, vertical collaboration through consideration of the value chain approach is incorporated. The Beneluxa Initiative, for instance, first performs horizon scanning to identify medicines that could be of interest for collaborative action, then conducts a joint HTA, which may be followed by a joint negotiation. Similarly, FINOSE recently used its latest joint assessment report to invite pharmaceutical companies to enter a joint negotiation process with procurement functions in five Nordic countries (Denmark, Iceland, Finland, Norway and Sweden) (14).
Annex 2. References


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2 All references accessed 1–2 May 2022.


The WHO Regional Office for Europe

The World Health Organization (WHO) is a specialized agency of the United Nations created in 1948 with the primary responsibility for international health matters and public health. The WHO Regional Office for Europe is one of six regional offices throughout the world, each with its own programme geared to the particular health conditions of the countries it serves.

Member States

Albania  Greece  Portugal
Andorra  Hungary  Republic of Moldova
Armenia  Iceland  Romania
Austria  Ireland  Russian Federation
Azerbaijan  Israel  San Marino
Belarus  Italy  Serbia
Belgium  Kazakhstan  Slovakia
Bosnia and Herzegovina  Kyrgyzstan  Slovenia
Bulgaria  Latvia  Spain
Croatia  Lithuania  Sweden
Cyprus  Luxembourg  Switzerland
Czechia  Malta  Tajikistan
Denmark  Monaco  Türkiye
Estonia  Montenegro  Turkmenistan
Finland  Netherlands  Ukraine
France  North Macedonia  United Kingdom
Georgia  Norway  Uzbekistan
Germany