Novel policy options for reimbursement, pricing and procurement of AMR health technologies

Final report

Commissioned by the Global AMR R&D Hub

Gesundheit Österreich
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This report contributes to the implementation of the 2030 Agenda for Sustainable Development, in particular to Sustainable Development Goal (SDG) 3 “good health and well-being” and its target 3.8 “Achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all”.

Executive summary

Background and aim

Antimicrobial resistance (AMR) is a global health threat. A key pillar in the multi-faceted approach to tackle AMR includes the development and commercialisation of novel antibiotics to replace those to which patients are increasingly becoming resistant. Another approach is focused on diagnostics, which, among others, help decide whether or not the prescription of an antibiotic is required, thus reducing antibiotic consumption.

Medicines and medical devices, hereinafter referred to as health technologies, usually enter the market of a country after the public authority has decided whether, and to what extent, the cost of the specific health technology will be paid for by the public payer. Linked to these reimbursement and procurement decisions, the price of the health technologies can also be determined by authorities. **AMR health technologies have special characteristics** such as a dearth of data and evidence, a value to society higher than added therapeutic benefit, and comparably low prices of antibiotics compared to diagnostics. These considerations are not yet well captured by the current standard policies on reimbursement, pricing and procurement. There is a need for a more finely tuned set of specific policy options.

Against this backdrop, the study aimed to **identify specific policy options in reimbursement, pricing and procurement that are able to incentivise production and market entry of AMR health technologies (novel antibiotics and diagnostics)**. Included are examples of national policies already in place for AMR health technologies as well as for health technologies with similar characteristics.

Methods

The study surveyed existing national policy options for **AMR health technologies and further health technologies** (medicines and medical devices) **with similar characteristics** in the so-called peri-launch stage (between marketing authorisation and market entry). This concerns the policy areas of **reimbursement** (funding), **pricing** and **procurement**. Policies of both **outpatient and inpatient sectors** were considered. A taxonomy of standard policies and of exemptions, incentives and deviations (**specific policy options**) was developed as a basis for the analysis.

Ten countries were examined: Australia, Brazil, France, Germany, Italy, South Africa, Saudi Arabia, South Korea, Spain and Turkey. These are G20 members (or a "permanent guest" in the case of Spain). They are balanced with regard to geography, demography, income, health and pharmaceutical system characteristics and pharmaceutical market size.

For the case study countries, information as of 2020 was **surveyed with representatives of pharmaceutical pricing and/or reimbursement authorities**. The respondents were asked to review a country fact sheet that had been pre-filled based on (grey) literature, including unpublished pieces of information (e.g. shared within the Pharmaceutical Pricing and Reimbursement Information / PPRI network). They were additionally invited to answer detailed questions in order to help identify

and understand examples of specific policy options. **Written responses** were received from all ten countries, and open questions were clarified in follow-up interviews or in written correspondence.

Further examples of specific reimbursement, pricing and procurement policies for AMR and similar health technologies **in other countries** were explored through literature review.

Identified policy options were **assessed** with regard to their benefits, risks and **transferability to AMR health technologies**, taking the specific challenges of these products into account.

Results

Reimbursement

Reimbursement relates to the decision of a public authority as to whether the expenses for the use of a health technology by the patient are paid by the public payer, and to what extent. All ten countries take **reimbursement decisions at national level** for most medicines, and for a few medical devices in eight of the study countries (however, these health technologies may be procured by public purchasers). If designated eligible for reimbursement, in all ten countries these health technologies are included in a **reimbursement list** which allows **individual reimbursement**. As a rule, countries do not offer individual reimbursement for health technologies procured for hospital use but they are financed as part of the bundled funding of a diagnosis-related groups (**DRG**) system.

To support the reimbursement decision (as well as the pricing decision, frequently performed in the same process), authorities in all ten countries perform **Health Technology Assessments (HTA).** In an HTA, the cost-effectiveness of the health technology is studied, taking into consideration its (added) therapeutic benefit (i.e. clinical outcome parameters, usually compared to an alternative). HTA differ from the regulatory assessment for the decision on granting marketing authorisation.

Specific policy options to privilege health technologies similar to AMR health technologies include the **inclusion into reimbursement despite little or no evidence**, faster access into reimbursement through **early access schemes** and **add-on funding**. **Privileged health technologies** include orphan medicines, oncology medicines, medicines that are considered "innovative", medicines locally developed and - rarely also - novel antibiotics.

A pathway for the inclusion of a health technology with little or no evidence into reimbursement is through **exempting** it **from HTA** (i.e. waiving the cost-effectiveness analysis requirement). This incentive has been applied for defined health technologies in Australia, Germany, South Korea and Turkey. The exemption from an assessment means missing the opportunity to collect data. An alternative is to modify the methodology, including criteria for consideration in the assessment. Some countries (e.g. Spain) consider AMR as one of several factors in their HTA. To move forward, countries may consider **adapting** their **value assessment framework** to better capture the value of AMR health technologies (e.g. societal value). This can build on previous work of targeted value assessment frameworks developed for other health technologies (e.g. for orphan medicines) and ongoing research.

Another example of preferential funding for defined health technologies is **additional funding through dedicated budgets**, such as the "innovation funds" in Italy or the Cancer Drug Fund in England. Experience has shown unintended effects of these budgets, such as growing public spending over time and no improvement to access cost-effective health technologies in cases when the additional funding is not linked to any assessment. A variant to consider in the context of AMR health technologies is to **"carve-out" defined health technologies from** the bundled **DRG** funding system and to finance them on an individual basis (e.g. the "liste en sus" in France, the "NUB" list in Germany and similar examples in non-study countries). Despite similar risks as for dedicated budgets, this specific policy option might be beneficial as it incentivises hospitals to purchase more expensive novel antibiotics. Clear rules and conditions should be attached to this model.

Pricing

Reimbursable medicines (i.e. those funded by public payers) are **price-regulated** in eight of the ten study countries, and price regulation is applied for all medicines in the remaining two countries. In four study countries, **some reimbursable medical devices** are also **price-regulated**. Price regulation means that the pricing authority sets the price, in contrast to free pricing where the supplier determines the price.

Germany constitutes an exemption: manufacturers are allowed to launch a medicine at a freely set price immediately after marketing authorisation. This price is unconditionally paid by German social health insurance for the first twelve months. Afterwards, if the medicine qualifies for remaining in reimbursement, its initial price is changed to a price informed by the outcomes of an HTA.

When the authorities set the price, they apply different criteria for different types of health technologies, resulting in **different pricing policies** (**combinations of pricing policies** are possible). For new technologies, countries compare the prices of the same health technology in other countries (policy of **external price referencing** – applied for medicines in all ten study countries and for medical devices in two countries). Prices of the identical or similar health technologies in the same country are considered for health technologies with competitors (**internal price referencing** – for medicines in all ten case study countries and for medical devices in five countries). Production costs are rarely considered for pricing for new medicines (**cost-plus pricing** – exceptionally used for medicines in three countries but not for medical devices). In addition, value (usually defined as "therapeutic benefit") based on an HTA process is frequently considered in pricing and reimbursement decisions for new health technologies. This is a kind of **value-based pricing** policy – applied for medicines in ten of the study countries and for medical devices in three countries. For new health technologies, especially in the case of high prices, the decision process is accompanied by **negotiations**, which usually relate to both the price and reimbursement (negotiations for medicines in all ten study countries and for medical devices in six countries).

Higher prices (including "**premium prices**") are typically granted for higher therapeutic benefits, but other criteria (e.g. preference for local production in South Korea) may also be considered. Allowing MAH and suppliers to freely set the price at their own discretion only offers an incentive in cases of the **ability-to-pay** on behalf of the purchasers. Thus, reimbursement which is secured by public funding is an important supportive factor.

Procurement

Public procurement of health technologies, i.e. purchase for use in public health care institutions, can take different forms depending on the type of the technology (e.g. monopoly product versus one among several competitors, low- versus high-volume technology). In organisational terms, procurement can be **done at facility level** (procurement of some or most medicines and medical devices in all ten study countries) **or pooled** at regional or centralised levels. All ten study countries perform procurements at central level (either through a national procurement agency, the NHS or a social insurance institution) for some medicines with high prices and uncertainty and/or for health technologies used in hospitals. The scope of health technologies subject to central procurement differs (e.g. Brazil, Saudi Arabia and South Africa procure most health technologies centrally).

In public procurement of health technologies, **tenders** are a common procurement method, and the lowest-priced bid is rewarded. Over the years, **new procurement tools** have been developed and applied in some countries. These tools constitute a move away from a purely price-based approach to more **value-based procurement**. Concern that a "race-to-the-bottom" in price competition may contribute to shortages was one major motivation for these reforms. Examples of new procurement methods, as allowed by EU procurement legislation, include the "**Most Economically Advantageous Tender**" / MEAT principle, which considers price as an important but not the sole award criterion, and electronic framework agreements based on the "dynamic purchasing system".

To ensure access to new health technologies with high budget impact and limited evidence on the clinical outcomes, all study countries except Brazil and South Africa have concluded **managed-entry agreements** (MEA) for medicines. Three countries have used them for medical devices, but rather seldom. While most MEA are financially-based (discounts, capping, price-volume agreements), performance-based MEA which link public funding to clinical outcomes are on the rise. MEA are most often concluded for orphan medicines and cancer medicines. MEA constitute a major administrative burden (negotiation of the deal, data collection and analysis, monitoring) and are flawed by their confidential character (secret discounts). This limited transparency of MEA sends wrong signals to other countries on the price level and further exacerbates the information asymmetry between the supplier and purchaser, thus further weakening the bargaining power of the latter. Despite these major disadvantages, MEA are considered as a useful option to allow patient access to health technologies that are otherwise unaffordable. They constitute a tool to "manage uncertainty" given limited evidence of health technologies as they allow data generation over time. As part of the agreement, specific conditions can be attached.

MEA might serve as a model policy option for AMR health technologies since, for instance, conditions on good stewardship might be built into an MEA. In two non-study countries, England and Sweden, pilots on procurement arrangements for novel antibiotics, in which payments by the public payer will be delinked from the volume, are currently being implemented. In the case study countries, a purchasing model with "**delinking**" the revenue paid from the volume was only identified in Australia, however not for AMR health technologies. The Australian "Netflix" model allows unlimited use of hepatitis C medicines at a fixed revenue across the country for five years.

To increase purchasing volume and to strengthen bargaining power, countries may consider **collaborating in joint procurement**. Brazil, together with other Latin American countries, is involved in pooled procurement through the PAHO Revolving Fund and the PAHO Strategic Fund, and Saudi Arabia is engaged in a procurement collaboration for essential medicines and medical supplies of the Gulf Cooperation Council. In Europe, there are experiences of joint procurement led by the European Commission, as part of the EU Joint Procurement Agreement for medical countermeasures and a recent experience of joint procurement of COVID-19 vaccines. Cross-country collaborations organised and led by national governments have also been emerging in Europe, but none of the European study countries is a member of a cross-country collaboration with joint procurement experience. Experience from the joint procurements of vaccines by the Baltic Procurement Initiative and of hospital medicines by the Nordic Pharmaceutical Forum are examples for successful procurements.

Conclusions

Overall, **countries apply a mix of different (standard and specific) reimbursement, pricing and procurement policies for health technologies**, which they have adapted to their policy objectives and needs. While few national reimbursement, pricing and procurement policies provide specific incentives to suppliers to launch AMR health technologies into national markets, this study has identified specific policy options in the study countries that provide **privileged access** pathways for **defined groups of medicines** (in particular orphan medicines and cancer medicines) which face similar challenges as AMR health technologies.

The policy options are **exemptions** from cost-containment (e.g. free pricing for suppliers, exemptions from mandatory discounts and claw-backs), **modifications** (e.g. higher prices and/or higher reimbursement rates for specific groups of health technologies, new procurement tools and purchasing contracts, such as managed-entry agreements and delinkage models), and **additions** in terms of supplementary funding sources (e.g. specific budgets and funding on top of the diagnosis-related groups system in hospitals).

It has been shown that, as a rule, specific reimbursement policies are able to address the **challenge of AMR health technologies** regarding their limited evidence, while specific pricing policies address the challenge of low prices, and specific procurement policies address the uncertainty regarding sales.

Promising models include **adapted value assessment frameworks (HTA)** that take into account the societal value and special characteristics of AMR health technologies and may eventually allow inclusion in reimbursement despite the absence of data and evidence in terms of added therapeutic benefit and **managed-entry agreements** or similar procurement contracts. The latter can include AMR relevant conditions (e.g. good stewardship, environmentally friendly) and possibly a **delinkage** model (payments independent from the sales volume).

These and further policy options may **serve as a model** to be adapted for fostering the launch and use of AMR health technologies in the national contexts.

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Abbreviations

ADL	Affections de longue durée / Long-term diseases
AEMPS	Agencia Española de Medicamentos y Productos Sanitarios / Spanish Agency for Medicines and Medical Devices
AIFA	Agenzia Italiana del Farmaco / Italian Medicines Agency
AMR	Antimicrobial resistance
AMS	Antimicrobial stewardship (programme)
ANSM	Agence nationale de sécurité du médicament et des produits de santé / French Medicines Agency
ATU	Autorisation temporaire d'utilisation (early access scheme in France)
BfArM	Bundesinstitut für Arzneimittel und Medizinprodukte / Federal Institute for Drugs and Medical Devices (Germany)
CDF	Cancer Drug Fund (England)
CEA	Cost-effectiveness analysis
CED	Coverage With Evidence
CEPS	Comité économique des produits de santé / Economic Committee for Health Care Products
CIPM	Comisión Interministerial de Precios de los Medicamentos / Inter-Ministerial Pricing and Reimbursement Committee (Spain)
CSP	Code de la santé publique / Public Health Code (France)
CSS	Code de la sécurité sociale / Social Security Code (France)
DAA	Direct acting antivirals
DBCAC	Drug Benefit Coverage Assessment Committee (South Korea)
DDD	Defined daily dose
DG SANTE	Directorate-General for Health and Food Safety (European Commission)
DPS	Dynamic Purchasing System
DRG	Diagnosis-related group(s)
EBM	Evidence-based medicine
ECDC	European Centre for Disease Prevention and Control
EMA	European Medicines Agency
EML	Essential medicines list
EPHA	European Public Health Alliance
EPR	External Price Referencing
ESMO-MCBS	European Society for Medical Oncology Magnitude of Clinical Benefit Scale
EU	European Union
EUnetHTA	European network for Health Technology Assessment
FAAP	Fair and Affordable Pricing
FDA	U.S. Food and Drug Administration
G20	International forum for global economic cooperation consisting of a group of twenty countries

G7	International informal forum for global economic cooperation consisting of a group of seven countries
GAP	Global action plan
GAVI	Global Alliance for Vaccines and Immunisation (former name, now: GAVI Alliance)
G-BA	Gemeinsamer Bundesausschuss / Federal Joint Committee (Germany)
GBP	Great Britain Pound
GCC	Gulf Cooperation Council
GDP	Gross domestic product
GEVIT	In vitro products Management (Brazil)
GGMED	General Office of Medicines (Brazil)
GGTPS	General Management Health Products (Brazil)
GKV	Gesetzliche Krankenversicherung / Statutory Health Insurance Funds
GÖ FP	Gesundheit Österreich Forschungs- und Planungs GmbH (subsidiary of GÖG responsible for delivering research and planning services to public institutions)
GÖG	Gesundheit Österreich GmbH / Austrian National Public Health Institute
GRADE	Grading of Recommendations, Assessment, Development and Evaluation
GUARD	Global Union for Antibiotics Research and Development
HAS	Haute Autorité de Santé / High Authority of Health
HE	Health expenditure
HIC	High-income country
HIRA	Health Insurance Review & Assessment Service (South Korea)
HPF	Hospital pharmaceutical formulary
HTA	Health Technology Assessment
ICER	Incremental cost-effectiveness ratio
IHPA	Independent Hospital Pricing Authority (Australia)
IMI	Innovative Medicines Initiative
INGESA	Instituto Nacional de Gestión Sanitaria / National healthcare management institute (Spin)
IP	Intellectual Property
IPR	Internal Price Referencing
IQWIG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen / Institute for Quality and Efficiency in Health Care (Germany)
IQWIG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen / Institute for Quality and Efficiency in Health Care (Germany)
IVD	In vitro diagnostic
JPA	Joint Procurement Agreement (European Union)
KCDC	Korea Centers for Disease Control and Prevention (South Korea)
KHEntgG	Krankenhausentgeltgesetz (Law for Funding of Hospitals in Germany)
LCSP	Ley de Contratos del Sector Público (Public Sector Procurement Code in Spain)

LEEM	Les Entreprises du medicament (pharmaceutical industry association in France)
LMIC	Low- and middle-income country / countries
MAH	Marketing authorisation holder
MBS	Medicare Benefits Schedule (Australia)
MDR	Multidrug-resistant
MEA	Managed-entry agreement
MEAT	Most Economically Advantageous Tender
MEDEV	Medicines Evaluation Committee of the European Social Insurance Platform
MER	Market Entry Reward
MFDS	Ministry of Food and Drug Safety (South Korea)
MoCA-OMP	Mechanisms of Coordinated Access to Orphan Medicinal Products
MoH	Ministry of Health
MOHW	Ministry of Health and Welfare (South Korea)
NEML	National Essential Medicine List
NHIS	National Health Insurance Service (South Korea)
NHS	National Health Service
NICE	National Institute for Health and Care Excellence (England)
NPM	Non-prescription medicine(s)
NUB	Neue Untersuchungs- und Behandlungsmethoden / new diagnostic and treatment methods regulation (Germany)
OECD	Organisation for Economic Co-operation and Development
OMP	Orphan medicinal product(s)
OOP	Out-of-pocket payments
PAHO	Pan American Health Organization
PBS	Pharmaceutical Benefits Scheme (Australia)
PCT	Procalcitonin test
POC	Point-of-care
POM	Prescription-only medicine(s)
PPP	Purchasing purchasing price (wholesale price)
PPRI	Pharmaceutical Pricing and Reimbursement Information (network of competent authorities of pharmaceutical pricing and reimbursement in more than 50 countries)
PR	Pricing and reimbursement
PRA	Pharmaceutical Reform Agreements (Australia)
PRP	Pharmacy retail price
PRV	Priority Review Voucher
R&D	Research and Development
RCT	Randomised control trial(s)
REA	Relative Effectiveness Assessment
RKI	Robert Koch Institute
RWD	Real-world data
RWE	Real-world evidence

SAHPRA	South African Health Products Regulatory Authority
SCMED	Secretariat of the Medicines' Market Regulatory Chamber (Brazil)
SFDA	Saudi Food and Drug Authority (Saudi Arabia)
SHI	Social Health Insurance
SNS	Sistema Nacional de Salud / National Health Service (Spain)
SSI	Social Security Institution (Turkey)
SUS	Sistema Único de Saúde / National Healthcare System (Brazil)
TIPR	Transferable Intellectual Property Rights
TITCK	Turkish Medicines and Medical Device Agency
TPP	Target Product Profile
TVF	Transparent Value Framework
UHC	Universal Health Coverage
UMIC	Upper-middle income country
UNCAM	Union nationale des caisses d'assurance maladie / National Union of Health Insurance Funds
US	United States (of America)
USD	United States dollar(s)
VAT	Value added tax
VBP	Value-based pricing (as such used in this study) / value-based procurement
VODI	Value for Diagnostics Information
WHA	World Health Assembly
WHO	World Health Organization
XDR	Extensively drug-resistant

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1 Background

1.1 Global challenge of antimicrobial resistance

Antimicrobial resistance (AMR) is a global public health issue that is accountable for deaths and complications in treatment [1–3]. 700,000 annual deaths are a commonly quoted figure [4] but the exact number of annual global deaths is unknown [5]. In addition, AMR-related death and follow-up treatments also have important economic implications for the health system [6–8].

It has been noted with concern that no major **new class of antibiotics** has been discovered since 1987 and too few antibacterial agents are in development to meet the challenge of multi-drug resistance [9]. According to a review of the World Health Organization (WHO), 50 antibiotics and combinations (with a new therapeutic entity) were in the clinical antibacterial pipeline in September 2019. Since July 2017 only eight antibiotics have been released to the market providing only little additional clinical benefit [10].

At the same time, it has been observed that well-established **"old" antibiotics** have increasingly been subject to shortages and/or have been withdrawn from the market [5, 11]. While shortages are known to be, in general, an increasing problem globally [12–16], concerns have been raised about low prices (e.g. as a result of competitive pricing policies such as tendering) as a possible factor that national markets lose attractiveness for suppliers [17, 18].

The pipeline for supply for new **fast diagnostic tests**, which would allow point-of-care (POC) testing and quick results (within minutes) for the decision on whether, or not, the prescription of an antibiotic is indicated [19–21], is also considered insufficient [4, 5]. In addition, for diagnostics, which are now available, there are issues of uptake given their specific features (cf. chapter 1.3.2).

In May 2015, in response to the AMR crisis, the World Health Assembly (WHA) adopted a **global action plan (GAP) on antimicrobial resistance** [9, 22]. One of its five strategic objectives is to develop the economic case for sustainable investment that takes account of the needs of all countries and to increase investment in new medicines, diagnostic tools, vaccines and other interventions.

Regional and national documents add to these global frameworks. More than a decade ago, the Conclusions of the Council the European Union of 1 December 2009 on innovative incentives for effective antibiotics recognised a significant decline in research into and development of new effective antibiotics and identified an urgent need to create incentives for research and development of new antibiotics, especially in those areas where the need is greatest [23]. The EU Action Plan on Antimicrobial Resistance from 2017 [2] highlighted a need for new economic models to incentivise antimicrobial discovery and development as well as for the development and uptake of novel diagnostics, taking into account the relatively high price of diagnostics compared to the currently low price of antimicrobials.

At the national level, the "O'Neill report" (UK Review on AMR [4]) in 2016 and the German GUARD report in 2017 [24] are well-known documents that analyse the global AMR challenges and propose recommendations.

1.2 Approaches to tackle AMR

To tackle AMR in a sustainable manner, **multi-faceted approaches** are required.

A **key strategy** is to ensure a more appropriate use of antibiotics [25]. In addition to the tools of antimicrobial stewardship (AMS) programmes [10, 25-29], fast diagnostic tests can support clinical decision-making by the identification of possible resistance and susceptibility issues, by avoiding unnecessary use and thus more targeted use.

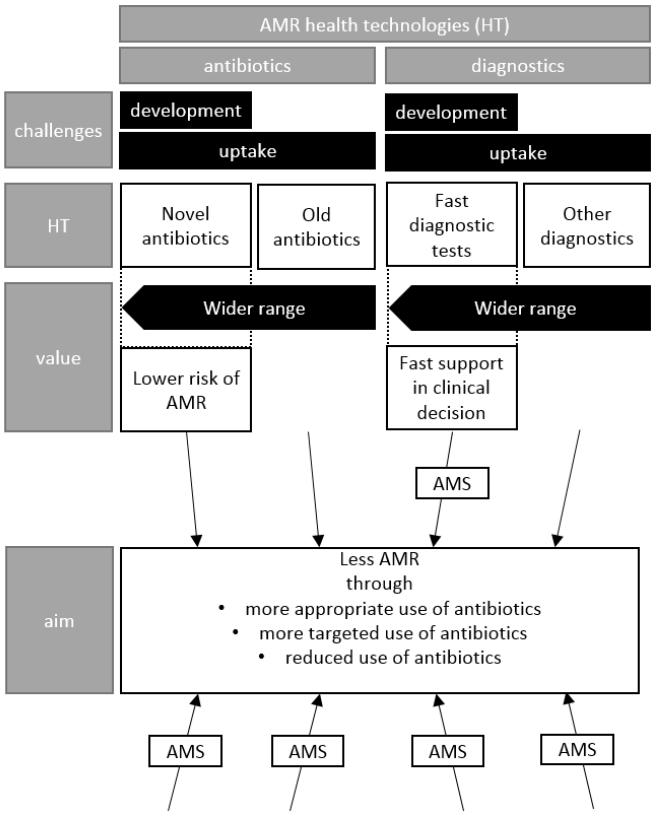
Figure 1.1 provides a simplified illustration of a few possible approaches, with a focus on the role of the (new) health technologies. Relevant health technologies in the context of AMR ("AMR health technologies") include novel antibiotics with a lower probability to produce AMR as well as (rapid) diagnostic tests.

Up to now, most recommendations in the field have focused on **incentives for** research and development (**R&D**) **for novel antibiotics**. For more than a decade, models to incentivise research in antibiotics have been proposed. They included a range of pull, push, so-called lego-regulatory and hybrid measures [30-38]. Several proposals have concerned funding support for R&D[1] and IP-based incentives[2].

[1] E.g. direct research funding through grants or forgivable loans, tax incentives, such as credits, allowances or deferrals for research and development expenditures, product development partnerships

[2] E.g. Priority Review Voucher (PRV, i.e. vouchers granted for the development and approval of certain priority medicines that can be redeemed to expedite review of a medicine that would not normally qualify for priority review) and market exclusivity action through Transferable Intellectual Property Rights (TIPR)

Figure 1.1:
Background – Role of health technologies among the multi-faceted approaches to tackle AMR



AMR = antimicrobial resistance, AMS = antimicrobial stewardship (programme), HT = health technologies, med. = medicines, MD = medical devices

Source and presentation: GÖ FP based on literature including [1, 2, 4, 19, 25, 35]

However, a 2016 report noted critically that "presently, there are few antibiotic initiatives that target the commercialization aspect of the antibiotic value chain. These include the three end prizes for diagnostic tools and the market exclusivity extensions offered by drug regulatory agencies to qualified antibiotics" [34]. But it seems that these tools do not **incentivise commercialisation** [30, 32], and new incentives have been called for to reward the commercialisation of new antibiotics that address unmet public health needs [10–13] by "paying for the innovation rather than utilization" [39]. Among projects, the recently concluded Innovative Medicines Initiative (IMI) project DRIIVE-AB aimed to develop solutions to stimulate antibiotic innovation and to ensure that these new antibiotics are used sustainably and are available equitably [21, 40, 41]. In contrast, suggestions that focus on incentivising the market entry and uptake of diagnostics are rather rare. The current IMI project "VALUE-Dx" aims to **demonstrate the value of diagnostics** to combat AMR [42].

To incentivise commercialisation of novel health technologies, "premium pricing" was suggested, using the outcome-based pull mechanism of **market entry rewards** (MER). MER are monetary prizes for the development and approval of a health technology (usually in the context of antimicrobials)

that meets a target product profile (TPP) and thus addresses a specific medical need [32, 41, 43]. The rewards could also be made conditional on certain aims. These would include commitment to antimicrobial stewardship, equitable and affordable access, contribution to diagnostic development, sales reporting to health authorities, surveillance of resistance levels, etc.) [4, 24, 41, 43]. And these could be designed with partial or full "delinkage" of the MER recipient's revenue from sales volume [38]. Proposals for MER include the suggestion for the Global Innovation Fund for AMR in the UK Review on AMR ("O'Neill report" [4]) and the Global Launch Reward as suggested in the GUARD report [24]. A major challenge of MER is the cost: estimations range between 10 and 30 billion USD for a 10-year programme bringing 10 to 15 novel antibiotics to the market [4, 41, 44]). MER funding at this scale could, in reality, be only achieved through pooling of funds of several governments and further institutions.

Thus, MER and several further suggestions presented in the literature and policy debate are still **"blue skies" policy ideas** which do not yet have precedent nor a clear global administrative structure through which they could be realised.

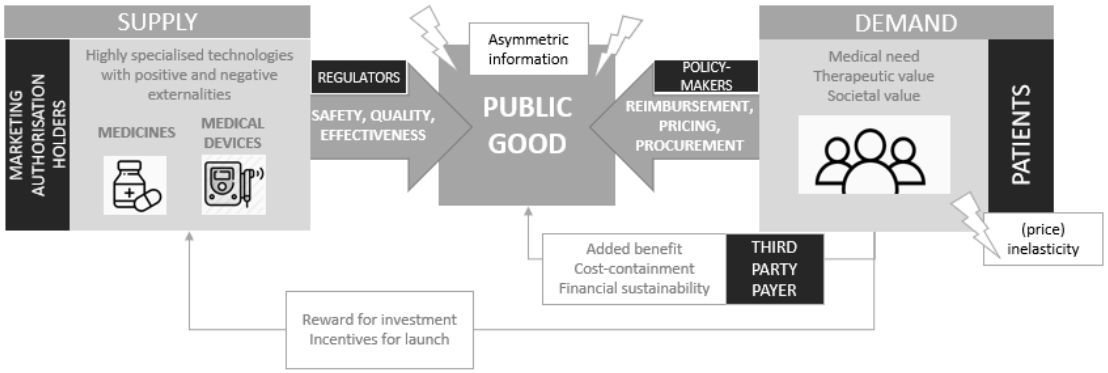
Given the pressure for action, there is an increasing openness and an appetite to consider further **policy tools** beyond incentives for R&D. These policies include those which are the competence of national governments and which have **already** been **implemented in the policy areas** of reimbursement, pricing and procurement. Reimbursement, pricing and procurement based on "value" have been proposed [36, 44-49] to take into account the specific characteristics of AMR health technologies, as presented in the next chapter.

1.3 AMR health technologies

1.3.1 Characteristics of health technologies

Medicines and medical devices are not "normal" commodity goods but are examples of "public goods" with particular specificities [50] (cf. Figure 1.2).

Figure 1.2:
Background – Specificities of health technologies



Source: GÖ FP based on literature including [30, 32, 50, 51]

First, medicines and medical devices offer value to patients and society, thus – in economic terms – they provide **positive externalities** [30, 32]. Their benefits may go beyond the treatment of the specific patient as further societal areas (e.g. the labour market, the tax system) also benefit from positive clinical outcomes. Societal value may not be seen immediately but can occur later in time (discounting). Policy-makers have to address the challenge to assess the value of "future health" when they decide on a health technology to support.

Second, however, health technologies also have **negative externalities** because their use implies **risks** (e.g. advent events, AMR) [30, 32]. Thus, medicines and medical devices (in particular those of higher risk categories) have to comply with safety requirements before they are allowed to enter the market. Clinical trials are strictly **regulated** to ensure the safety of included study participants as much as possible. Regulatory authorities (such as medicines agencies) play a major role as "door openers" for the launch of medicines into national markets, and they monitor safety during use (pharmacovigilance).

Third, health technologies are frequently highly developed "goods", a fact which hinders an assessment by "outsiders": Suppliers of health technologies know more about their product than public authorities, who assess the technologies for different purposes: e.g. to grant marketing authorisation (safety, effectiveness and quality aspects) or to decide on the price which the public payer will pay (procurement, pricing and reimbursement decision). In addition, there is **information asymmetry** on benefits and risks between the health care providers, who recommend its use, and the patients.

Fourth, there is **low price elasticity** in the demand for health technologies. It may even become completely inelastic in life-threatening and other serious situations (e.g. children requiring medical treatment), when the patient or family member is willing to pay any price.

Fifth, in solidarity-based health care systems, the "normal" interaction between seller and purchaser is supplemented by the inclusion of a **third party**: The patient uses the health technology

but neither pays nor decides on its use, while the health care provider (doctor) decides on a patient's use of a health technology funded by a (public) payer.

1.3.2 Specificities of AMR health technologies

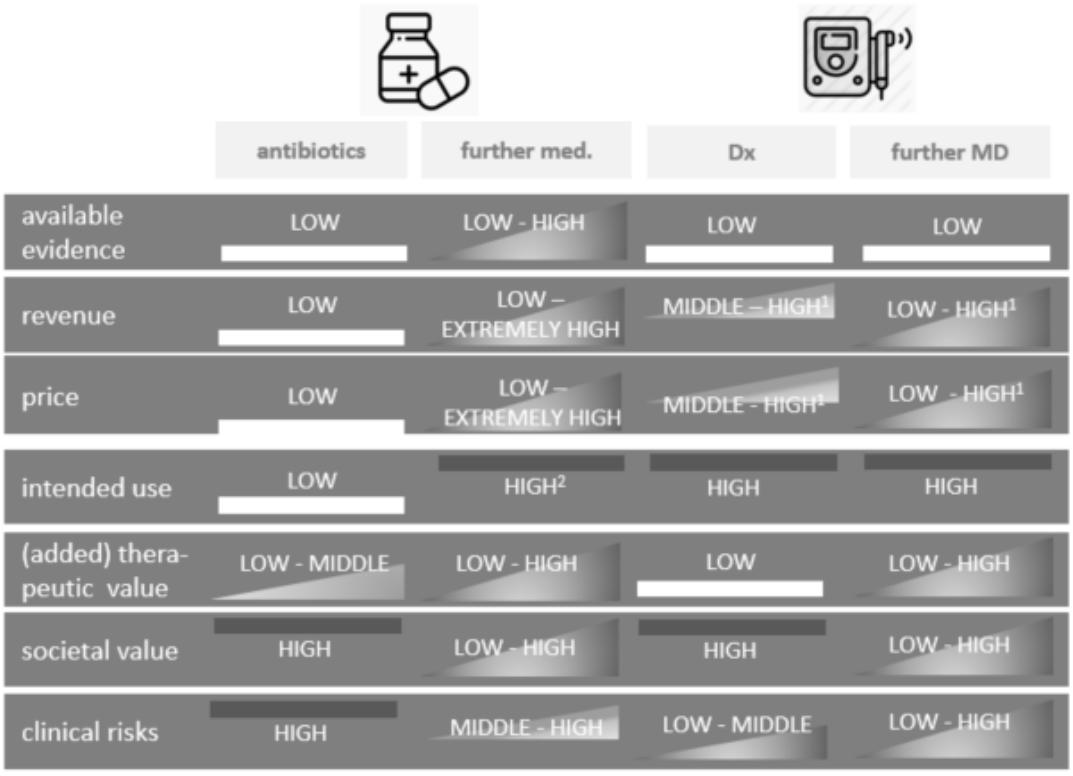
For the purpose of this study, AMR health technologies include the following:

» antibiotics (well-established and novel antibiotics) and

» diagnostics to determine if the infection is caused by a virus or bacteria (e.g. lab-related diagnostics and rapid diagnostic tests that allow POC use at doctors and in pharmacies).

In addition to the above-mentioned characteristics of health technologies (positive and negative externalities, information asymmetry, low price elasticity and three party relationship), further aspects come into play that are specific to AMR health technologies (cf. Figure 1.3).

Figure 1.3:
Background – Specificities of AMR health technologies in relation to other health technologies



Dx = diagnostics, MD = medical devices, med. = medicines
[1] but lower than for medicines
[2] in accordance with guidelines

Source: assessment by GÖ FP based on literature including [49, 52]

Unique characteristics, also in comparison to other health technologies, are:

» Only relevant for antibiotics: The **use** of antibiotics is aimed to be kept as low as possible and required.[3]

» This results in rather low **volumes**, also due to the fragmented demand for antibiotics (usage for short-term curative treatment).

» Established antibiotics are rather low-**priced**, also in contrast to the diagnostic tests [4].

» Expected **revenues**, in particular for antibiotics, are rather low, given the restrictions in intended use, fragmented demand and low(er) prices.

» Available **evidence** on the (added therapeutic) value of AMR health technologies is rather low, per health technology group for different reasons:

  » The value of a health technology (in particular of a medicine) is usually assessed through (added) therapeutic benefit, i.e. the advantage of a medicine in clinical outcome parameters compared to alternatives. As the antibiotic market offers a range of similar therapeutic options, even novel antibiotics will likely show only limited added therapeutic value. The societal value, however, is more difficult to capture in the traditional tools of "value assessment" and especially in reimbursement and pricing policies based on these assessments (cf. chapter 1.4). There are further medicines groups (e.g. orphan medicines) which show similar characteristics and suffer from the same challenges (see below, cf. Table 1.1).

  » Medical devices, including diagnostic tests, are overall less subject to regulation (to prove safety and quality) and to specific reimbursement, pricing and procurement policies for which they are required to demonstrate (therapeutic and/or societal) value.

  However, health technologies with societal value do not necessarily demonstrate high therapeutic value (therapeutic benefit).

Finally, in the AMR health technology market, there is another particularity: Antibiotics and diagnostics constitute a kind of a **pair** as they complement each other, since diagnostic tests help determine whether, or not, antibiotics should be prescribed and if yes, which antibiotics. The uptake of antibiotics and diagnostics might even be conflicting: "The use of diagnostics represents a classic example of a 'public good': the benefits are better antibiotic conservation and slower development of resistance and accrue to society at large over time, while the near-term costs are incurred by individual doctors or patients. It is simply more expensive and more time consuming for a doctor or a patient to use a diagnostic than to use a drug 'just in case' it is needed, even if a test could help save costs and reduce waste at a health system-wide level, and help preserve the usefulness of antibiotics for all, over the longer-term. Many drug companies, meanwhile, including those producing affordable generic antibiotics, have no commercial interest in the advent of rapid diagnostics, which would act to limit the number of antibiotics prescribed."[4].

---

[3] However, it should be noted that for several medicines prescribing guidelines also offer guidance in prioritisation (e.g. first-line, second-line therapy) and provide restrictions (e.g. regarding duration and repeated use, focus on or exclusion of defined patient groups) for clinical purposes.

1.3.3 Challenges for AMR health technologies

Based on their specificities, AMR health technologies face several challenges:

» **To prove their value** (either therapeutic or societal value):
  » **Lack of data (evidence)** at the time of market entry which would be a prerequisite for demonstrating value for reimbursement, pricing and procurement decisions (for diagnostics large randomised control trials (RCT) are performed rather seldom; for antibiotics and further medicines different data are required for reimbursement, pricing and purchasing decisions than for marketing authorisation, but clinical trials are often focused on the data generation for marketing authorisation (cf. chapter 1.4).
  » **Mismatch** between value of AMR health technologies and **commonly used "value assessment" frameworks**, which are focused on added therapeutic benefits and thus limited differentiation from other health technologies [52]
  » Due to the novelty, **lack of real-world data (RWD)** and real-world evidence (RWE) which could be supportive for demonstrating societal value

» **To generate the sufficient revenue** for suppliers
  » Limitations due to **overall low prices** of that group of health technologies
  » Limitations due to a **lower price** of a health technology compared to the price of competitor technologies (e.g. in competitive settings)
  » Due to **low volumes** (e.g. resulting from good stewardship programmes)

» **To ensure "planning certainty",** which is important for suppliers
  » Limitations in planning due to their specificities as either short-course curative treatment (antibiotics) or ad-hoc use (diagnostics)

» To be subject to a **fragmentation of the health system**
  » Use and funding in different settings (e.g. outpatient and inpatient sectors) with different policy environments
  » Mixture of national, regional and local policies

AMR health technologies are not alone in having to meet these challenges; other groups of health technologies also struggle to address these challenges (cf. Table 1.1). Some challenges (e.g. the fragmentation in the health system) are relevant for all health technologies.

Table 1.1:
Background – Challenges for AMR and further health technologies

Challenges	AB	Dx	OMP	Vaccines	Sp. med.	G / Bios
1. To prove value						
1a. Lack of data	Y	Y	Y	Y	Y	N
1b. Mismatch to value assessment frameworks	Y	Y	P[1]	Y	P[1]	N
1c. Lack of real-world data	Y	Y	P	Y	P	N
2. To generate the sufficient revenue to suppliers						
2a. Overall low prices	Y	P	N	P	N/A	Y
2b. Lower prices than those of competitor medicines	P	N	N	P	N/A	Y
2c. Low volumes	Y	P	Y	P	N/A	N/P
3. To ensure "planning certainty" to suppliers	Y	P	Y[2]	N[2]	Y[2]	P
4. Subject to a fragmentation in the health care system						
4a. Different settings (outpatient/inpatient)	P[3]	P[3]	P[3]	P[3]	P[3]	P[3]
4b. National, regional and local level	P[3]	P[3]	P[3]	P[3]	P[3]	P[3]

AB = antibiotics, Bios = Biosimilars, Dx = diagnostics, G = generics, N = No, N/A = information not available, i.e. no assessment possible, OMP = orphan medicinal products, P = partially, sp. med. = specific medicines (certain indications), Y = Yes

[1] Mismatch for OMP (and oncology OMP) that common value assessments do not sufficiently capture specificities (e.g. societal value) of these medicines was addressed by the development of specific value (assessment) frameworks (e.g. Transparent Value Framework (TVF) of the Working Group on Mechanism of Coordinated Access to Orphan Medicinal Products (MoCA-OMP) for orphan medicines [53, 54], cf. Box 4.2, the European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS) for oncology medicines and further frameworks [55])

[2] Limited planning certainty in case of medicines and vaccines for ad-hoc needs (e.g. acute treatment, epidemic)

[3] Less related to the type of health technology but rather to the organisation of the health care system

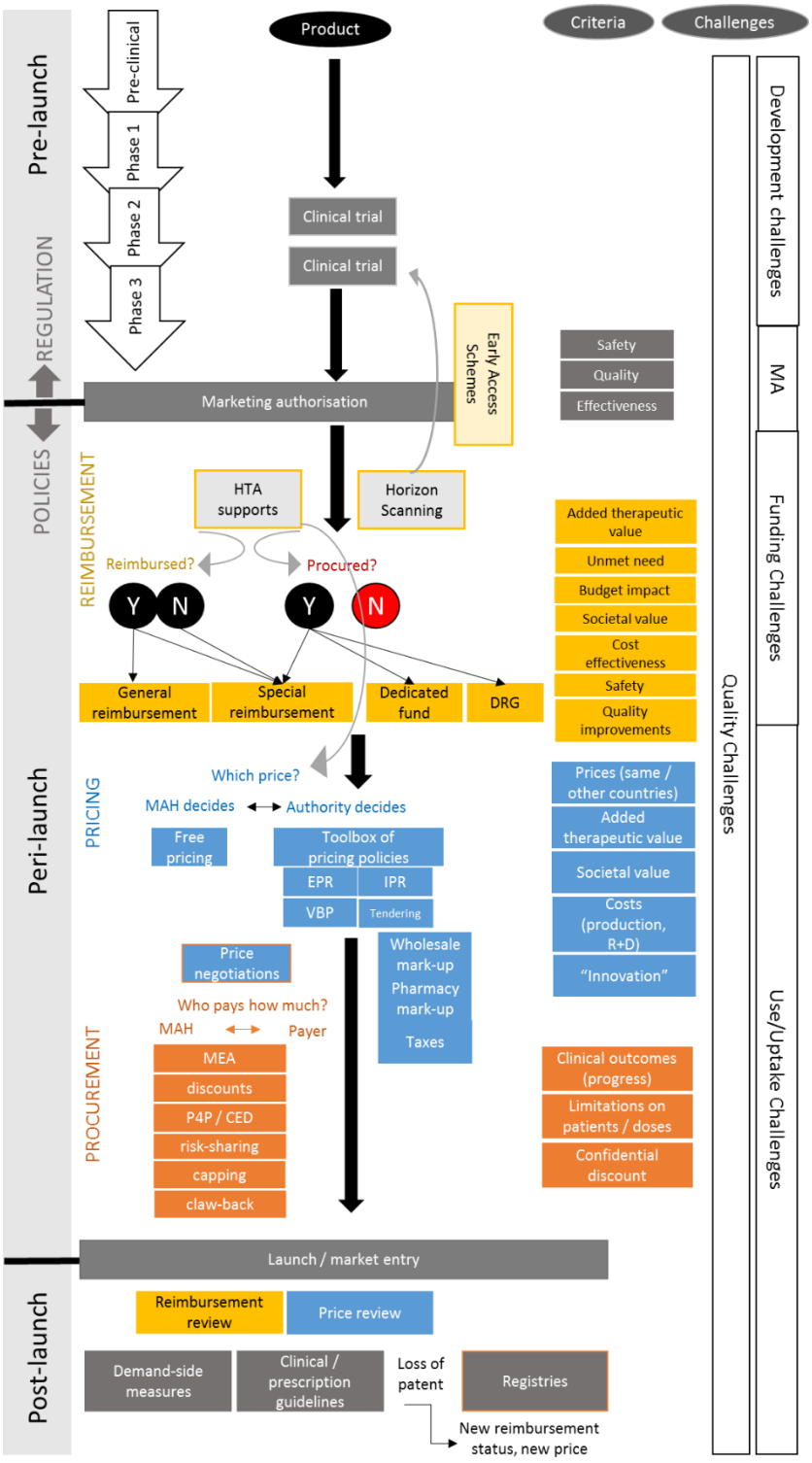
Source and presentation: GÖ FP based on literature [45-49, 56]

1.4 Pathway of health technologies through the system

The use of a health technology by a patient is the result of a long process. Figure 1.4 provides a simplified illustration of this process for a new medicine. The assumed settings are (highly) developed with a high degree of regulation (to ensure quality and safety) and a wide range of reimbursement, pricing and procurement policy options laid down in legislation. Different policies may be implemented for different groups of medicines (e.g. specific indications; special designation such as for orphan medicines; high-budget impact, high-value, prescription-only or reimbursable medicines) and in different settings (outpatient and inpatient; national, regional and local levels).

In principle, the path of a medical device, including a diagnostic, through the system can be similar. However, the level of regulation as well as the extent of reimbursement and pricing policy implementation is, in general, lower for medical devices than for medicines [57-60].

Figure 1.4:
Background – Sequential path of a health technology through the system illustrated for a new medicine in a regulated policy environment



CED = Coverage with Evidence, DRG = diagnosis-related groups, EPR = external price referencing, IPR = internal price referencing, MAH = marketing authorisation holder, MEA = managed-entry agreement, P4P = Pay-for-Performance, VBP = value-based pricing
Simplified illustration based on assumptions: a health care system in which third party payers (public or private payers) may cover (part of) the expenses of the health technologies
No specification made on whether, or not, these policies are solely national ones; some reimbursement, pricing and procurement policies may also be implemented at regional and/or local levels
Presented policies are options of a "tool box"; not all of them are necessarily implemented in parallel for one medicine.
The sequence of policies in the peri-launch stage is country-specific and may differ from the one presented in this figure.
The policy areas of reimbursement, pricing and procurement are overlapping, and specific policies can also be attributed to another policy area.

Source and presentation: GÖ FP based on literature including [61-70]

On its way through the system (which is commonly called "value chain") a medicine passes three key phases: pre-launch, peri-launch and post-launch stages. They are divided by milestones:

» **Marketing authorisation** (between pre-launch and peri-launch stage): The medicine meets the regulatory requirements necessary for market entry.[4] However, this "theoretical passport for market entry" does not necessarily imply immediate launch of the health technology (thus no immediate patient access), since in many countries a medicine must have a decision on its reimbursement status and a price (reimbursement price) before it can actually be brought into the market.

» **Launch / market entry:** The medicine has been granted a price and awarded reimbursement (under certain conditions) and can now be marketed. It is still the discretion of the marketing authorisation holder (MAH) to do so, thus to decide on whether, or not, the medicine will actually be made available to the patients of a country.

This study is focused at the **peri-launch stage**, which is the period between the marketing authorisation and the actual launch (market entry) of a medicine. This stage which could even be considered as a kind of prolonged pre-launch stage may last between 0 days (in cases of immediate launch upon marketing authorisation when the authority does not take any price or reimbursement decision or grants a price and awards reimbursement without any assessment) and several months and even years [71, 72]. In the European Union, public authorities are obliged to take the decision on reimbursement and pricing within 180 days [73]. There is no deadline for a MAH to submit a price and reimbursement dossier or to launch a medicine.

The decisions to be taken in the peri-launch stage and policy options available are parts of the policy areas of reimbursement, pricing and procurement [61, 74]. These areas are overlapping (in some countries, e.g. Sweden, the decision on pricing and reimbursement is taken in the same procedure [75]), and some policies could also be attributed to another policy area as well.[5]

[4] There is differentiation per type of health technology. For instance, generic and biosimilar medicines may not be requested to demonstrate the effectiveness through clinical trials but a proof of bioequivalence and biosimilarity can be considered sufficient. For medical devices including diagnostics, a certification process can be in place instead of marketing authorisation.

[5] For the purpose of this study, for instance, managed-entry agreements (MEA) were subsumed under procurement since they represent specific purchasing contract options. In other studies, MEA are considered as reimbursement policies [64],

Box 1.1:
Background – Different requirements for the marketing authorisation and for reimbursement and pricing decisions

To be granted **marketing authorisation**, a medicine must prove its (1) **safety**, (2) **quality** and (3) **effectiveness** ("three hurdles"). This can be demonstrated by comparing it to placebo.

Afterwards, however, in the **reimbursement / procurement and pricing** process, the medicine must overcome the so-called "fourth hurdle": It must demonstrate its **superiority to alternatives** (usually other medicines; in some countries / cases, non-pharmaceutical alternatives may also be allowed) in order to be granted a higher price (compared to alternatives) and/or to be procured or be included into reimbursement. In several countries, national legislation also allows the inclusion of a medicine into reimbursement in the case of non-superiority but at the same or lower price of alternative medicines; there is no added therapeutic benefit but an "economic advantage".

More and different data are required for the decisions taken on reimbursement, pricing and procurement than for the decisions on the marketing authorisation status of a medicine. While the **added therapeutic benefit** and **cost-effectiveness** of a medicine are major guiding principles for reimbursement decisions and price comparisons support pricing and procurement decisions (cf. Figure 1.4), criteria expressing a broader understanding of **"value"** (e.g. societal value, unmet need) have also been defined in some national legislations.

More **early scientific dialogue** between reimbursement / pricing authorities and MAH is important, so that in the clinical trials the requirements for pricing and reimbursement can already be considered and the required data collected. However, in several cases, needed data cannot be sufficiently gathered in the clinical trials, and **real-world evidence** (RWE) would be needed, which can only be collected at later stages.

Source: GÖ FP based on literature including [64, 67, 69, 70, 76]

When a medicine has successfully passed the regulatory hurdle of marketing authorisation, it has then to **demonstrate its "value"** to be included in reimbursement (i.e. to be funded by a third party payer) or to be purchased by a public entity (e.g. federal state, region, public hospital, public procurement agency).[6] It is key to understand that the requirements (criteria) for marketing authorisation differ from those requested in the reimbursement, pricing and procurement processes (cf. Box 1.1).

and there is also the understanding of MEA as a pricing policy option for medicines with high budget impact. Each classification is correct since MEA include procurement, reimbursement and pricing elements. These missing standards in terminology and classification are attributable to the novelty of the pharmaceutical system research and pharmaceutical policy analysis disciplines.

[6] In specific cases (e.g. low-priced non-prescription medicines), a marketing authorisation holder may opt for not requesting reimbursement as this may offer other benefits (e.g. flexibility on the price; no statutory pricing in several countries [65, 77]).

The reimbursement authority and/or the procurement body are usually guided by an assessment (evaluation) of the health technology in question. Depending on the characteristics of the product (e.g. high-budget impact, novelty) and the capacity of the authority, these evaluations may vary regarding their comprehensiveness. In general, they include, at least, clinical and economic assessments. These evaluations are called **Health Technology Assessments (HTA)**. HTA are not pricing or reimbursement policies per se, but are supportive tools to inform authorities and procurers. According to the EU collaboration on HTA, EUnetHTA (for background information cf. Box 4.1), a full HTA would also include analyses of the cost and economic effectiveness, ethical aspects, organisational aspects, patient and social aspects, and legal aspects, whereas a "Rapid Relative Effectiveness Assessment" (REA) would be focused on the investigation of the health problem and the current use of the studied health technology, its technical characteristics, safety and clinical effectiveness [78]. National legislation defines which criteria and dimensions are considered for reimbursement and pricing decisions.

If a medicine has passed the next hurdle and is considered reimbursable (i.e. selected for inclusion in public funding) or eligible for being procured by the state, it can be funded through different mechanisms:

» **General reimbursement**: (Partial) coverage of the price of the medicine and included in a "general" reimbursement list

» **Specific reimbursement**: Similar to general reimbursement for which the medicine is not eligible but it is included in a separate reimbursement list (to ensure reimbursement for defined medicines which would otherwise be included in a tariff-based funding system)

» **Bundled funding mechanism**: A medicine is not individually reimbursed but paid as part of overall funding for services. A commonly used type is the diagnosis-related groups (**DRG**) system commonly applied in hospitals, in which hospital services are paid based on cases (tariffs), regardless of the cost to the hospital to provide services. This may result in hospitals avoiding to use higher-priced, potentially innovative medicines and other health technologies [79, 80].

» **Separate funds**: Medicines are financed through specifically established budget for certain medicines which would otherwise not be eligible for reimbursement. England's Cancer Drug Fund (CDF, cf. also Box 4.3) is an example for such a fund, which finances cancer medicines even if they are not cost-effective (normally a criterion for funding) [81-83].

Another step in the pathway through the system concerns the **decision on the price** of the medicine. Depending on the country and the type of medicine[7], this decision is either taken by the MAH or the pricing authority (or procurement agency). Different criteria, including prices of the same medicine in other countries, of similar medicines in the same country and "value" considerations (mainly added therapeutic value), are applied.

[7] In solidarity-based systems, the price of reimbursable medicines is usually set by a government authority [65, 84].

Price negotiations between the pricing authority and the MAH are a pricing (and procurement) policy that falls somewhere between statutory pricing by the authority and free pricing. In particular for medicines with high price tags and no or limited evidence, so-called **managed-entry agreements (MEA)** offer a solution to allow early and conditional patient access. Negotiated conditions may include the improvement of the health outcomes of patients in so-called performance-based MEA, such as risk-sharing agreements, pay-for-performance, Coverage With Evidence (CED) or conditional pricing. Flat discounts, price-volume agreements or capping (of doses or patients) have been negotiated in financially-based MEA. A common feature of MEA is the confidentiality of the negotiated conditions, including the net price [64, 68, 85-87].

While reimbursement, pricing and procurement policies are mainly located in the peri-launch stage, there are some "borderline" policies and tools leaking into the pre- and post-launch stages respectively:

» **Horizon scanning:**

  Horizon scanning (or an early alert system) is a tool used by public authorities (usually payers) to identify early potential candidates of medicines that require attention (e.g. promising to address unmet need but with high budget impact). Horizon scanning allows payers to be prepared and to do the prioritisation accordingly.

  This is the most common application of horizon scanning, looking into the pre-launch phase. A variant of horizon scanning is, however, to monitor the possible patent expiry of medicines (looking into the post-launch phase) to be able to react quickly and adapt.

» **Early access schemes**:

  These allow the use of medicines before their marketing authorisation under defined conditions.

  In addition to its regulatory components (ensuring safe use), early access schemes are also linked to the reimbursement system. Under an early access scheme, MAH may provide medicines for free to the patients, or they may be granted funding. The price under an early access scheme may be free but after the end of the scheme the price may be statutorily set and the difference in expenses between the free price and the set price might be subject to pay-backs of the MAH to NHS.

» **Reimbursement and/or pricing reviews:**

  After market entry of a medicine, authorities are encouraged to perform regular reviews to validate whether, or not, the reimbursement decision and the price of the medicine still meets the set criteria in light of new evidence and developments.

» **Registries:**

  Performance-based MEA may be accompanied by (patients or product) registries. While registries support monitoring the "success" of the treatment as a basis for the decision on the continuation of funding, they also collect important data to address regulatory issues (e.g. quality concerns) as well as efficacy data (use in real-world settings) to address uptake challenges.

1.5 Aim and scope of the study

Pricing, reimbursement (funding) and procurement contribute to incentivising the development and uptake of new antibiotics and diagnostic tests [21, 32], but there appears to be a lack of knowledge for policy-makers related to the (mix of) policy options to use. **It has not yet been studied which reimbursement, pricing and procurement policy options have the ability to incentivise production and market entry of AMR health technologies. Little has been published on the implementation of these policies for AMR health technologies.** One exemption is a recently published study which surveyed reimbursement policies to tackle market failures for antimicrobials in five countries [88].

However, there are indications that a few **countries have implemented reimbursement, pricing and procurement policy options** (or adjusted the design of existing policies) with the aim to incentivise the market entry of novel antibiotics and diagnostics, and thus their development and production. In addition, it can be anticipated that specific approaches have been developed and/or implemented **for further health technologies** which face similar challenges as the novel antibiotics and diagnostics (cf. chapter 1.3.1). Some of these policies could be used as a "blue print" for pricing, reimbursement and purchasing of novel antibiotics and diagnostics.

It should be possible by **drawing from the learnings** on AMR health technologies and further health products of high societal value in different countries from various regions of the world, to identify new or alternative policy options and concrete paths for the future.

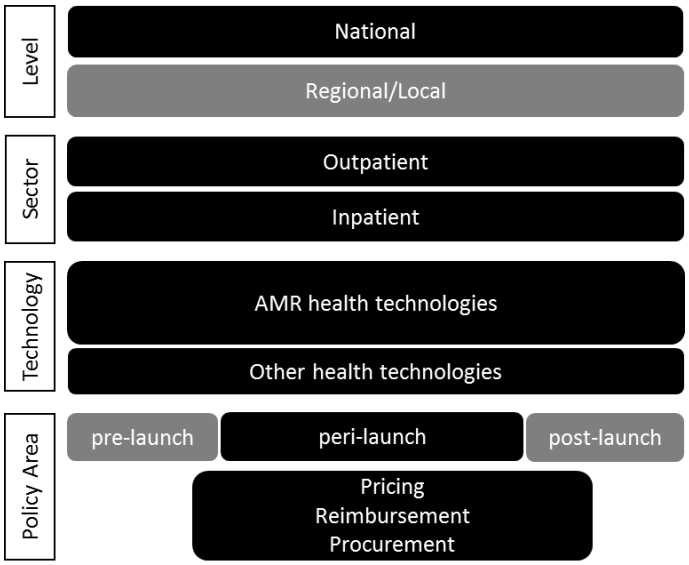
Against this backdrop, the present **study identifies national policy options in reimbursement (funding), pricing and procurement that incentivise the market entry of health technologies.** They may relate to (novel) antibiotics or diagnostics and also, and in particular, to other medicines and diagnostics with similar characteristics.

This study investigates policies that have already been implemented in national contexts in the areas of reimbursement, pricing and procurement. It thus explores **peri-launch policies** taken between the marketing authorisation (or certification) and market entry. Policies which relate to earlier or later stages in the value chain (pre-launch and post-launch measures) are only considered in case of a link to the peri-launch stage (e.g. early access schemes, cf. chapter 1.4).

According to the Terms of Reference in the call for tender [89], this research was originally planned to be addressed in two studies: a study on "cost-containment exceptions" (i.e. reimbursement and pricing policies) and a second one on "purchase contract options" (i.e. procurement). Since both topics are interlinked, it was decided to merge them into the present single study. In addition, the study that had initially been intended to focus on the **hospital sector** has been extended to include the **outpatient sector** as well. Thus, it covers the actual situation in many countries where the range of policies implemented in the outpatient sector is broader and several policies are not specific to one sector and are applied in both sectors.

The study is focused on **national** policies that are relevant for a whole country. While acknowledging that regional policies may play a major role in some countries, with strong regional health systems, their existence is mentioned, if applicable and relevant, but have not been further investigated.

Figure 1.5:
Background – Scope of the study



Source GÖ FP

The study run from February 2020 to December 2020.

2 Methods

The study aims to identify the reimbursement, pricing and procurement policy options for medicines and medical devices which are able to incentivise production and market entry of AMR and similar health technologies. In doing so, reimbursement, pricing and procurement policies that have been implemented in selected case study countries and beyond were surveyed and assessed with regard to their transferability to AMR health technologies.

2.1 Selection of case study countries

The study covers a selection of **10 countries** of the G20 group (with Spain as a "permanent guest") from all continents except North America. Three countries are upper-middle income countries (UMIC), while the other seven are high-income countries. Three countries are part of the G7 and major developed economies, two further countries have developed economies and the remaining five countries are classified as having developing economies. The selected case study countries are well-balanced with regard to the selection criteria. The latter include general characteristics in terms of geography, demography and income of the countries as well as specificities of the health care system and health spending and the pharmaceutical market, including its size. Key data of these countries are presented in Table 2.1 and described in further details in chapter 7.1.1 in the Annex.

2.2 Survey

A multi-step approach was chosen to survey information on policies in the selected case study countries (Figure 2.1).

Based on a broad literature and data review which also considered unpublished information (e.g. shared within the Pharmaceutical Pricing and Reimbursement Information / PPRI network, for details on sources see chapter 7.1.2), a fact sheet following an homogeneous structure (cf. chapter 7.1.3 in the Annex) for each country studied. It contained a description of standard and specific policy options for medicines and medical devices in outpatient and inpatient sectors (in accordance with the scope of the study, cf. chapter 1.5) and contained detailed questions to identify and understand examples of specific policy options. The authors chose the approach of pre-filling fact sheets instead of an empty questionnaire, as made it possible to validate – sometimes contradictory – information available in the literature and/or communicated by experts. In addition, it was intended to reduce the workload for the country experts.

Country fact sheets were sent to country experts in the field of pricing, reimbursement and procurement for written validation. In general, different experts were approached the areas of medicines and medical devices.

Table 2.1:
Methods – Characteristics of case study countries included, 2020

Characteristics	Australia	Brazil	France	Germany	Italy	Saudi Arabia	South Africa	South Korea	Spain	Turkey
Part of G20 countries	yes	yes	yes	yes	yes	yes	yes	yes	permanent guest	yes
Geographic area	Asia Pacific	South America	Europe	Europe	Europe	Middle East	Africa	Asia	Europe	Europe/ Asia
World Bank income group	HIC	UMIC	HIC	HIC	HIC	HIC	UMIC	HIC	HIC	UMIC
UN development class	developed economy	developing economy	major economy (G7)	major economy (G7)	major economy (G7)	developing economy	developing economy	developing economy	developed economy	developing economy
Number of inhabitants, in thousands (2019)	25,364	211,050	67,060	83,133	60,297	34,269	58,558	51,709	47,077	83,430
GDP (current USD), in million USD (2019)	1,392,681	1,839,758	2,715,518	3,845,630	2,001,244	792,967	351,432	1,642,383	1,394,116	754,411
Current HE, in % of GDP (2017)	9.21	9.47	11.31	11.25	8.84	5.23	8.11	7.60	8.87	4.22
Private HE, in % of current HE (2017)	31.09	58.05	22.91	22.34	26.10	33.29	44.39	42.62	29.38	22.29
Pharmaceutical expenditure, in % of HE	13.82 (2017)	7.80[1] (2008)	13.03 (2018)	14.20 (2018)	17.96 (2019, p)	18.00[2] (2010)	N/A[3]	N/A[4]	15.31 (2018)	27.81 (2000)
Antibiotic consumption, in DDD per 1,000 inhabitants per day	N/A	22.75 (2016)	25.92 (2018)	11.49 (2015)	21.40 (2018)	N/A	N/A	27.68 (2015)	17.96 (2015)	38.18 (2015)

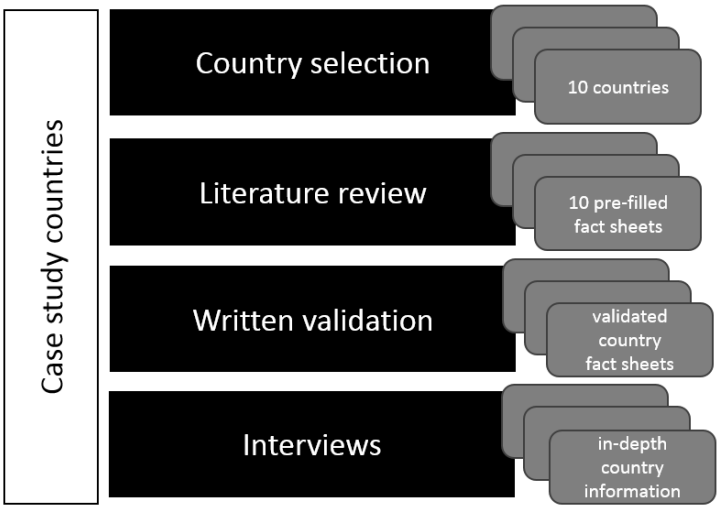
DDD = defined daily dose; GDP = gross domestic product; HE =health expenditure; HIC = high-income country, N/A = information not available, p = provisional value. UMIC =upper-middle income country, USD = US dollar

[1] Private health expenditure accounts for around two thirds of total health expenditure in Brazil. In the private market, medicines make up for around 30% of private health expenditure from households [90, 91]. [2] Total pharmaceutical expenditure in Saudi Arabia in 2010 was at 3.5 billion USD, which accounted for around 2% of the GDP. In 2010, around 60% of the pharmaceutical expenditure was covered privately [92]. [3] In South Africa, the private sector is dominating for pharmaceutical expenditure making up for around 84% of total pharmaceutical expenditure. Yet, the public health sector serves health care needs of around 84% of the population while only accounting for 16% of total pharmaceutical expenditure. [4]In South Korea, pharmaceutical expenditure amounted to around 21.7 trillion South Korean won in 2014, with the public sector accounting for up to around 57% [93].

Further sources not mentioned in notes: [20, 94–99]

Information was received via e-mail, mostly in the form of commented pre-filled fact sheets containing more information, notes and responses to questions in the email correspondence.

Figure 2.1:
Methods – Survey methods for the ten selected countries



Source: GÖ FP

After written validation, country experts were asked to participate in an interview to allow for verbal validation and possibly identify and discuss specific policy examples. Some country experts were available for telephone or online interviews, while others opted for having this second round of validation in written form. Interviews took between 45 and 120 minutes and were documented in minutes based on written notes.

The pre-filled fact sheets were validated for all ten countries (however, in some countries only for medicines and not or only partially for the medical devices sector), and country experts from five of the ten countries were available for an interview.

In addition to primary data collection in the ten case study countries, examples of specific reimbursement, pricing and procurement policy options for AMR and similar health technologies were explored **in other countries** through literature review.

2.3 Transferability of country information to global learnings

The aim of this study was to identify interesting and innovative examples of reimbursement, pricing and procurement policies of AMR health technologies and further technologies of similar characteristics and to consider their feasibility for serving as models for other countries (cf. chapter 1.5).

In doing so, the authors were confronted with challenges regarding the definition and specifications of "policies" (or policy options), because pharmaceutical reimbursement, pricing and procurement policy research is a rather new research area, and research on these policies for medical devices have started even more recently.

» *Lack of definitions*: Standards and definitions are lacking, and the same terms may be used with different interpretations. To contribute to more clarity, key technical terms used in this report are defined in a glossary (cf. chapter 7.3 in the Annex).

» *Overlapping policy areas*: A policy may target different, sometimes conflicting, policy objectives (e.g. reward for commercialisation of a health technology that addresses unmet need, financial sustainability of the health system), and it may also address more than one policy area (e.g. pricing and reimbursement).

» *Relevance of the design of a policy ("policy dimensions"):* In several cases, there is not "the" policy but the implementation of a policy can be designed differently.[8]

For the purpose of this study, the authors used the terms "standard policies" and "specific policies" (or policy options). While "standard policies" relate to common, rather high-level policy tools, specific policies may either describe further policies or refer to a special design of an existing "standard" policy (thus including "policy dimensions" or "policy elements").

This study explored **specific policies** (or elements of policies) in the areas of reimbursement, pricing and procurement which were considered to be able to incentivise the market entry of health technologies.[9] The authors use the terms "specific policies" (or "specific policy options"), "incentives" and – if applicable – "exemptions". Incentives for research and development are not the scope of the study, but a possible impact of incentives intended to foster market entry on research and development may not be excluded.

As explained above (cf. chapter 2.2), the country fact sheets were pre-filled based on a homogenous structure of key "standard policies" for reimbursement, pricing and procurement. To explore specific policy options, possible incentives and exemptions were highlighted (e.g. a separate column in the country's flowcharts describing the pathways for health technologies through the system, and focused questions were asked in writing and in the interviews). However, country-specific

[8] For instance, the pricing policy of external price referencing is based on the rationale of setting the price by considering the prices of that health technology in other countries. However, there is large headroom in the design of this pricing policy: choices can be made with regard to the reference countries, the way the benchmark price is calculated, consideration of discounts or use of the list price, weighting by volume data and economic indicators such as purchasing power parities, choice of exchange rate, etc. These choices impact outcomes, as research confirmed [100, 101]. Similarly, there are numerous ways to design managed-entry agreements, and which conditions to attach.

[9] It is acknowledged that for several policy options the impact on intended policy objectives is not known. Overall, in the policy system research for health technologies there is a dearth of evaluations [102].

characteristics have led to a situation where a policy option could be considered "standard" in one country and "specific" in other countries.[10]

The surveyed policy information for the ten study countries was critically analysed to identify certain patterns of policy options (incentives and exemptions), and a **taxonomy of "specific policy options"** was developed. In total, six specific reimbursement policies, five specific pricing policies and and five specific procurement policies were defined. Policy information identified through the survey and through literature in additional countries was categorised using the developed taxonomy. Since responses from the country experts in writing and in the interviews were received at different points in time, the **fine-tuning of the taxonomy** and the clustering of the policy options was a longer-lasting **sequential** process (cf. also chapter 2.4).

Assessment of the identified policy options, also with regard to possible transferability, was done based on evidence from the literature and policy experience of the authors. In particular, it was assessed if, and to which extent, identified policy options would be able to **meet the challenges of AMR technologies**. This analysis was informed by the experience of the implementation of specific policy options for health technologies with similar characteristics as AMR health technologies.

2.4 Limitations

The present study has some limitations. Several of them are linked to the challenges of the novelty of the discipline of policy system research and analysis for health technologies as described above in chapter 2.3: limited clarity due to lack of definitions, concepts and taxonomies; ambiguity with regard to policies which are importantly impacted by their design; and overlapping policy areas of reimbursement, pricing and procurement. Linked to this, the defined scope of the study (peri-launch stage) had to be extended in some cases due to "border-line policies" reaching into other stages (cf. chapter 1.4).

The study is not a comprehensive review, and it was never intended to be. It is rather a collection of specific policy options that may be beneficial for cross-learning. However, it is possible that further interesting and possible innovative examples are missing.

This is likely attributable to two major reasons:

First, specific policy options that were sought in this study concerned details and specificities in the system, and the country experts approached for validation did not always have knowledge at this level of detail. Despite generous support of country contacts to involve further experts, it was in particular difficult to find experts with such specific expertise for the medical devices sector. This may also result from the lower level of policy implementation for medical devices. In Turkey,

[10] Normally, MEA are quite specific purchase contract options. But in some countries (such as Italy and South Korea, cf. chapter 3.3) they are considered as part of the standard system.

the pre-filled information on policies for medical devices was not confirmed, and in Italy, this was only partially possible. Some specific examples identified in the literature could not be confirmed, and a few details were not examined.

Second, the sequential approach as described in chapter 2.3 (fine-tuning of the taxonomy for specific policies based on information generated in the study countries) might have contributed to a situation in which interesting examples were only identified at a later stage. If possible (e.g. interviews not yet done), the authors went back to the country experts to explore whether, or not, similar policies were also in place in their country. Upon presentation of preliminary findings to the commissioning body of this study, a change in the procurement policy taxonomy proved beneficial, and further specific procurement policies were included. However, these policies had originally not been surveyed in the study countries, so full coverage for all ten countries was not possible.

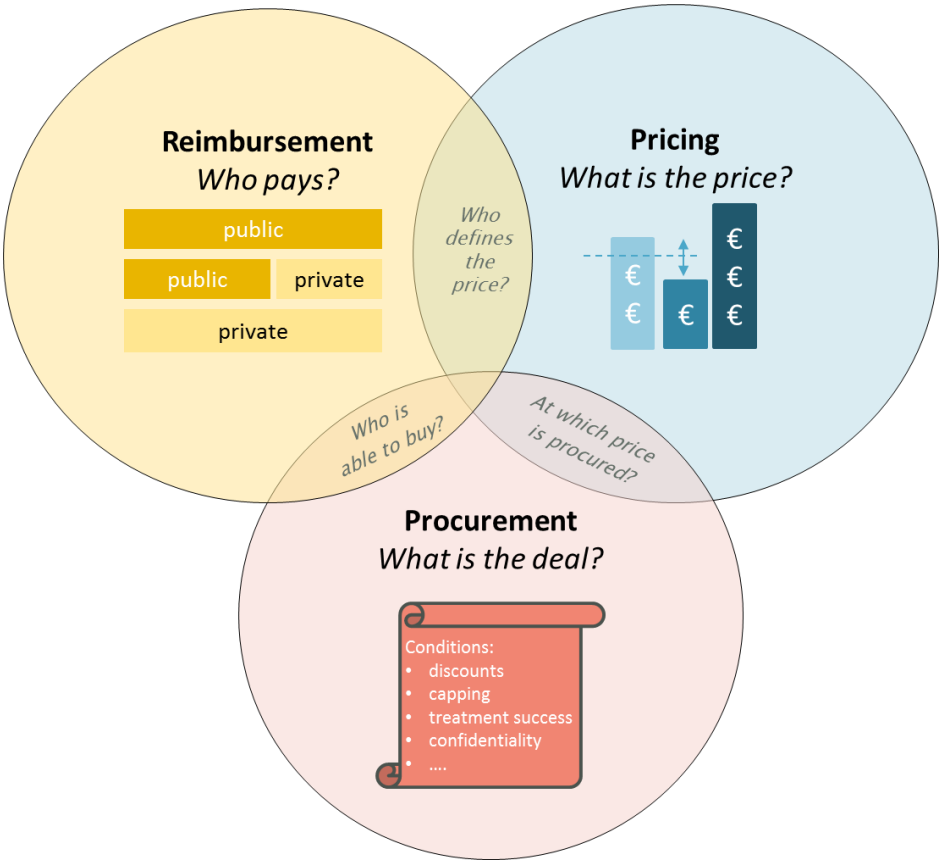
The study was performed for a sample of ten countries, based on defined criteria (see chapter 2.1). This approach might imply a selection bias as countries that could have provided further examples of specific policies (e.g. Sweden, UK) [49, 88] were not considered. To address this limitation, further examples from other countries identified in the literature were added in the discussion (cf. chapter 4).

Moreover, due to the COVID-19 pandemic, delays in written responses and availability of the experts for interviews were encountered in some cases.

3 Results

Reimbursement, pricing and procurement policies for health technologies (medicines and medical devices for the purpose of this study) are located in the so-called peri-launch stage of the "value chain", i.e. between marketing authorisation and market entry. As described in chapter 1.4, there are, however, a few "borderline" policies (e.g. horizon scanning, early access schemes). Reimbursement, pricing and procurement are overlapping (cf. Figure 3.1), and, as it will be seen in the course of this study, some policy options can equally be classified under a different policy area.

Figure 3.1:
Results – Reimbursement, pricing and procurement policy interlinkage



Source: GÖ FP

In designing these policies, policy-makers have to answer the following fundamental questions:

» **Reimbursement**: Who pays for the health technology – the (public) payer and/or the patient? How is the division of the financial burden? Which funding model (e.g. individual reimbursement of the health technology or bundled funding) is used? Which criteria are considered in the decision on the reimbursement?

» **Pricing**: Are prices of health technologies regulated (i.e. decided by the authority), or can the supplier decide? For which health technologies will the price be regulated? How high will be the price? Which criteria are considered in the decision on the price?

» **Procurement**: Is the government involved in purchasing the health technology? At which price? How, and on which criteria, are the winning offers selected? Which conditions and benefits of the health technology does the purchaser request from the suppliers? How is the decision taken and communicated? Do suppliers contribute to payments (e.g. in the form of rebates or claw-backs)?

The decisions on the **choice of policies and the design of these policies** are influenced by the overall policy objectives to be achieved. Some of these objectives are conflicting (e.g. reward for innovation for industry versus cost-containment, fostering competition versus security of availability of health technologies in the market, fast patient access versus evidence-based decision on reimbursement) [69].

While policies have been developed in a more advanced manner for medicines than for other health technologies, the same concepts are, in principle, also applicable for medical devices.

3.1 Reimbursement policies in the study countries

Reimbursement policies relate to government action as to whether or not a health technology (e.g. a medicine or a medical device) will be funded by a third party payer[11] (i.e. decision on the reimbursement status), and if yes, to which extent[12] ("reimbursement price") and under which conditions[13].

Figure 3.2 visualises the three major dimensions of coverage (i.e. scope of health technologies covered, scope of patients with access and extension of public funding) for health technologies based on the Universal Health Coverage (UHC) cube. This is based on the idea that for moving towards UHC, progress on all mentioned dimensions is needed.

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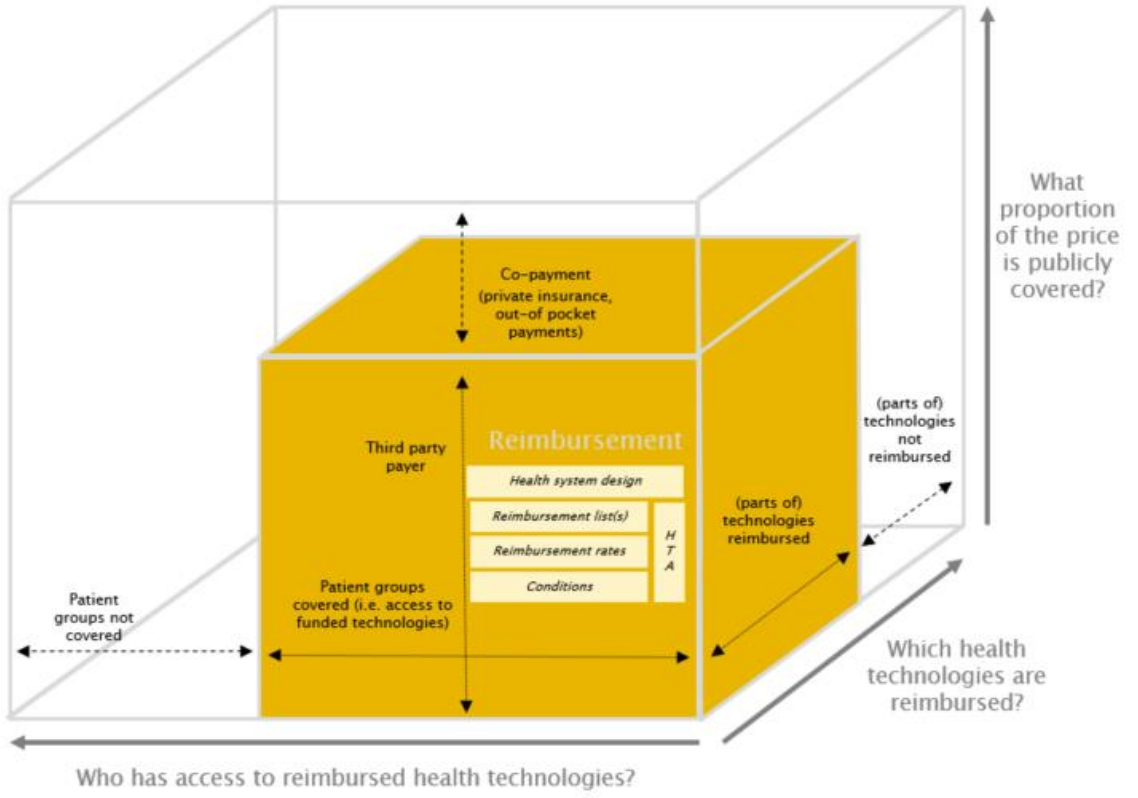
[11] It depends on the organisation of the health care system who the third party payer is: it may be the national health service (NHS), a social insurance institution and/or even a mutual social insurance and supplementary health insurance.

[12] A health technology may be fully funded by the state or third party payer. A health technology is considered reimbursable even if it is only partially funded by a third party payer. In such cases, co-payments are charged to patients. If a health technology is not reimbursed at all, then the patient has to cover all costs out-of pocket.

[13] Third party payers may decide and/or agree with the supplier to reimburse only defined specific indications and/or apply a defined cost-effectiveness threshold. These criteria may target the decision on the reimbursement status (whether or not to reimburse) as well as the extent of reimbursement. Furthermore, decisions on the status and extent of the reimbursement may vary across socio-economic groups (e.g. full reimbursement and exemptions from any co-payments for vulnerable groups) and across sectors (e.g. co-payments in the outpatient sector but full funding of a health technology in inpatient use).

Figure 3.2:
Results – Reimbursement policy framework



Source and presentation: GÖ FP based on the Universal Health Coverage (UHC) cube [103]

3.1.1 Standard reimbursement policies

Key decisions related to reimbursement (i.e. coverage of the cost of a health technology by a public payer) include:

» Is the health technology considered eligible for public funding? (decision on the **reimbursement status**)

» If yes, what is the division of financial burden between the public payer and the patient? (decision on the "**reimbursement price**")[14]

[14] Even if a health technology is eligible for reimbursement (so-called reimbursable health technology), co-payments may still apply for patients (e.g. in the form of a prescription fee, percentage co-payments or deductibles). For non-reimbursable health technologies, patients have to co-pay fully out-of pocket.

» Which criteria and tools are used to take a reimbursement decision? (e.g. role of HTA)

» Which **funding mechanisms** are used for financing reimbursable health technologies? (e.g. individual reimbursement of single health technologies included in a general or specific reimbursement list or through special dedicated budget and bundled funding as in DRG systems, see also chapter 1.4).

All ten study countries have a reimbursement policy framework for health technologies. For outpatient medicines there is a national **reimbursement list** (usually in the form of a positive list indicating those medicines included in reimbursement); a few study countries (e.g. Germany, Spain) also have a negative list. For medicines used in hospitals, reimbursement lists are also in place. The latter are either designed as a **national list** (e.g. in Brazil, France, Turkey) and/or **hospital pharmaceutical formularies** at the level of hospitals. In the case of both national list and hospital formularies, the latter are usually developed based on the national positive list.

There is an overlap between reimbursement and procurement, since the hospital pharmaceutical formularies tend to be rather indicative for procurement: medicines included in these lists are those selected to be procured for the hospitals. In South Africa, the National Essential Medicines List (NEML) indicates those medicines to be procured by the state for use in the public sector (free of any co-payments). Being "listed" does not necessarily imply **individual reimbursement of the health technology**. Medicines (and also medical devices) used in hospitals are usually funded through the tariff-based DRG funding mechanism (**bundled funding** per case), unless for defined exemptions, whereas listed outpatient medicines tend to be funded individually.

For some countries major **differences in the scope of the lists between medicines and medical devices** were reported as only a few groups of medical devices are eligible to be included in a reimbursement list.

Even for reimbursable health technologies **co-payments** can be charged for defined medicines and medical devices in outpatient use in some countries, for instance a fixed prescription fee for medicines in Australia, percentage co-payments of the price of a medical device in Turkey or a combination of fixed and percentage co-payments for medicines in France. In contrast, inpatients can access medicines and medical devices without any co-payment (except for South Korea).

All study countries reported to using **HTA as a supportive tool** for reimbursement decisions related to defined medicines. For medical devices HTA is not systematically used.

Table 3.1 provides an overview of the standard reimbursement policies in the study countries. Further details are provided in country-specific flow-charts in chapter 7.2 in the Annex.

Table 3.1:
Results – Standard reimbursement policies for health technologies of the ten study countries, 2020

Standard reimbursement policies		Reimbursement list(s)		Partial reimbursement for some reimbursable health technologies		HTA		Patient co-payments for reimbursable health technologies	
		Medicines	*Medical devices*	*Medicines*	*Medical devices*	*Medicines*	*Medical devices*	*Medicines*	*Medical devices*
Australia	outpatient	**National positive list**	**National positive list** (Medical Benefits Scheme)	**No** (all listed medicines 100% reimbursed)	**Partly** (up to 100% reimbursed)	**Yes**	**Yes**	**Yes, fixed** (fixed amount per perscription)	**Yes, %** (0/15/25% of health service)
	inpatient	**Hospital formularies** (managed by hospitals and state/territory governments)	**Hospital formularies** (managed by hospitals and state/territory governments)		**No**	**Not systematically** (some value assessment at state/hospital level)	**Not systematically** (some value assessment at state/hospital level)	**No**	**No**
Brazil	outpatient	**National positive list**	**National positive list**	**No** (all listed medicines 100% reimbursed)	**No** (all listed medical devices 100% reimbursed)	**Yes** (also for pricing)	**Yes** (except for diagnostics and other low risk medical devices)	**No**	**No**
	inpatient								
France	outpatient	**National positive list** (for medicines in outpatient use)	**National positive list** (with a section for medical devices in outpatient use and a section for medical devices in inpatient use)	**Yes** (depending on added therapeutic value)	**Yes** (depending on added therapeutic value)	**Yes**	**Yes**	**Yes, fixed and %** (prescription fee and % co-payment depending on therapeutic value, exemption for chronic diseases)	**Yes, %** (usually 40%)
	inpatient	**National positive list** (for medicines in inpatient use, additional lists for tow types of hospital medicines)		**No** (always 100% reimbursed)	**No** (always 100% reimbursed)			**No**	**No**
Germany	outpatient	**Negative list**	**Reimbursement list** (for treatment methods including medical devices)	**No** (all medicines not included in the negative list 100% reimbursed)	**No** (all listed medical devices 100% reimbursed)	**Yes**	**Yes** (mainly assesment of method, not device)	**Yes, fixed with % element** (10%, minimum 5 euro, maximum 10 euro)	**No** (except for medical aids & orthopaedics)
	inpatient	**Hospital pharmaceutical formularies** (at hospital level)	**Hospital formularies** (at hospital level)					**No**	**No**
Italy	outpatient	**National positive list** (with a section for medicines in outpatient use and a section for medicines in inpatient use; regional lists possible; HPF at hospital level)	**N/A**	**No** (all listed medicines 100% reimbursed)	**No** (all listed medical devices 100% reimbursed)	**Yes**	**Yes** (but not relevant as no reimbursement in outpatient use; no HTA for diagnostics)	**Yes, fixed** (prescription fee in most regions)	**N/A**
	inpatient		**Hospital formularies** (at hospital level)					**No**	**No**

Standard reimbursement policies		Reimbursement list(s)		Partial reimbursement for some reimbursable health technologies		HTA		Patient co-payments for reimbursable health technologies	
		Medicines	*Medical devices*	*Medicines*	*Medical devices*	*Medicines*	*Medical devices*	*Medicines*	*Medical devices*
Saudi Arabia	outpatient	**National positive list**	**National positive list**	**No** (all listed medicines 100% reimbursed)	**No** (all listed medical devices 100% reimbursed)	**Yes**	**Yes**	**No**	**No**
	inpatient								
South Africa	outpatient	**National Essential Medicines List** (as basis for procurement decision by state, NEML is kind of positive list in the public sector)	**Facility-based reimbursement lists**	**Partly** (medicines on state contract 100% reimbursed in the public sector)	**Partly** (medical devices 100% reimbursed in the public sector)	**Partly** (guideline on pharmacoeconomic assessment of high-priced medicines – not yet mandatory)	**No**	**Partly, fixed** (depending on the employment status of patients)	**No**
	inpatient								
South Korea	outpatient	**National positive list** (based on which hospitals establish and use own formulary)	**Negative list** (for the funding of medical devices and diagnostics	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**
	inpatient								
Spain	outpatient	**National positive and negative lists** (HPF at hospital and regional levels)	**Reimbursement list** (for few medical devices, not Dx)	**Yes**	**Partly** (few medical devices 100% reimbursed)	**Yes**	**No**	**Yes, %** (depending on socio-economic status, exemption for chronic diseases)	**Yes, %** (applicable only for a few medical devices, when reimbursed % co-payment)
	inpatient		**Hospital formularies** (at hospital level)	**No** (always 100% reimbursed)	**No** (always 100% reimbursed)		**No** (no HTA for medical devices included in DRG)	**No**	**No**
Turkey	outpatient	**National positive list** (for medicines in outpatient use)	**Positive lists** (specialty based for medical devices)	**Yes**	**Partly** (some medical devices up to 100% reimbursed)	**Yes**	**No**	**Yes, fixed and %** (prescription fee and % co-payment)	**Yes, %** (% co-payment)
	inpatient	**National positive list** (for hospital-only medicines)		**No** (always 100% reimbursed)	**No** (always 100% reimbursed)			**No**	**No**

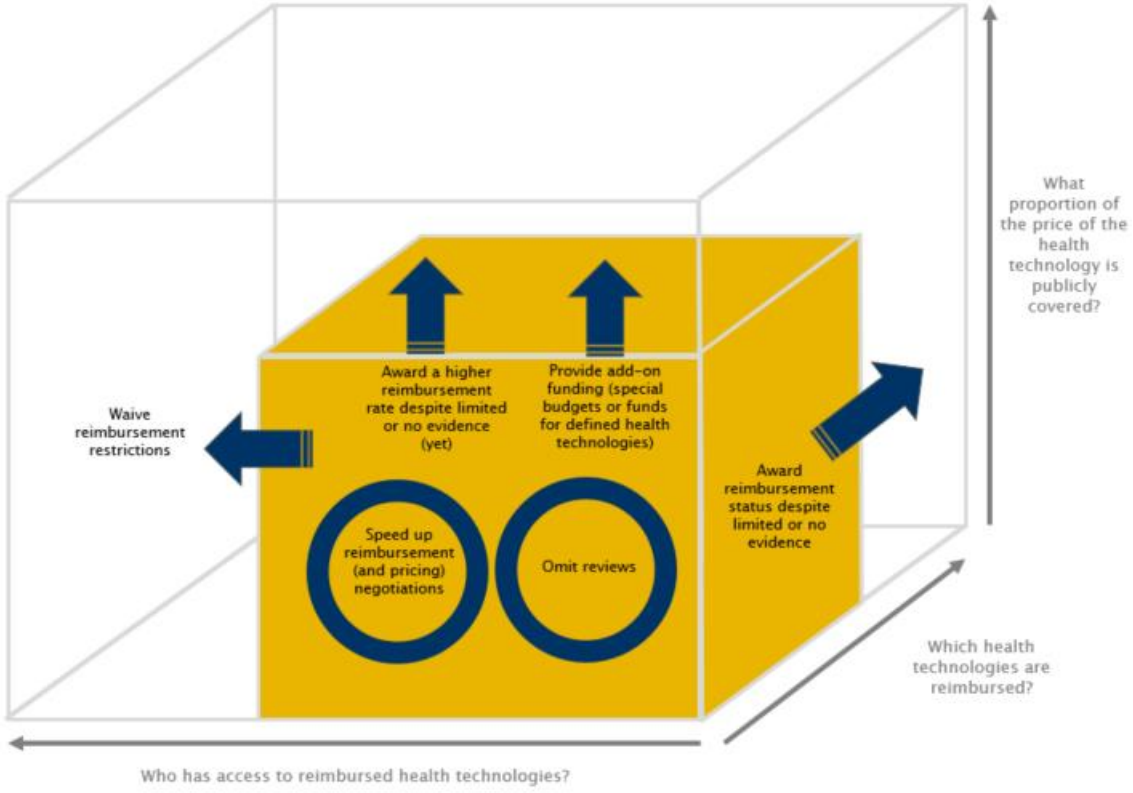
DRG = diagnosis-related groups (tariff-based funding mechanism mainly used in hospitals), Dx = diagnostic(s), HTA = Health Technology Assessment, SHI = Social Health Insurance

Source: GÖ FP based on literature and a survey with competent authorities of the countries

3.1.2 Specific reimbursement policies

In addition to common "basic" reimbursement policies, further policies could be implemented and/or the design of existing policies could be adapted to offer incentives to marketing authorisation holders and suppliers to bring their health technologies into the national markets.

Figure 3.3:
Results – Taxonomy of specific reimbursement policies



The figure is based on the Universal Health Coverage (UHC) cube which highlights the need for improvements in three dimensions (increase in patients covered, increase in health technologies covered, share of public funding) in order to make progress in UHC. An adaption of the UHC cube to reimbursement policies for health technologies is presented in Figure 3.2. The six identified specific policies are classified into the different areas of the UHC cube.

Source and presentation: GÖ FP based on the UHC cube [103]

The survey in the ten countries identified some specific policies (and adaptions to policies) in the area of reimbursement for health technologies. They can be clustered in six groups (see also Figure 3.3):

To **award** a **reimbursement status** for a health technology (despite limited evidence on its effectiveness, benefits, etc.; while, for instance, a similar health technology of similar efficacy and effectiveness is not reimbursed),
this includes taking a **decision** on reimbursement (status and rates) **without consideration** of available **evidence** (omission of HTA assessments) and with reduced assessment (limited HTA),

» To award a **higher reimbursement price / rate** for a health technology (despite limited evidence – in comparison to similar technologies),

» To take a decision in **early phases** before evidence can be assessed on time (fast-track reimbursement / early access schemes),

» To **omit regular reimbursement reviews** that might have resulted in possible exclusion from reimbursement (or lower reimbursement rates),

» To **waive** reimbursement restrictions that are linked to the **specific (prescribing) guidelines or conditions** of use and

» To use **add-on funding** mechanisms, e.g. special budgets or funds for defined technologies.

Table 3.2 offers an overview of examples for these six specific reimbursement policies. For medicines, a higher number of specific policies were found than for medical devices in the ten countries. Most specific reimbursement policies (for medicines in 7 countries, for medical devices in 3 countries) are implemented with the aim to ensure faster access in reimbursement (early access schemes). 8 countries have specific policies to grant access to medicines despite lack of evidence of added therapeutic benefit (and two countries for medical devices). The identified examples are presented in further detail in the chapters to come.

Table 3.2:
Results – Overview of specific reimbursement policies for health technologies of the ten study countries, 2020

Specific reimbursement policies	Inclusion in reimbursement list(s) despite limited evidence / therapeutic benefits		Higher reimbursement (rates) despite limited evidence/ therapeutic benefit		Faster access into reimbursement (easy access schemes)		Ommitting reimbursement reviews		Waiving reimbursement restrictions / conditions of use		Add-on funding (budgets)	
	MED	*MD*	*MED*	*MD*	*MED*	*MD*	*MED*	*MD*	*MED*	*MD*	*MED*	*MD*
Australia	■				■				■			■
Brazil	▫	▫										
France	■		■		■	■	▫				■	
Germany	■	■			■					■	■	■
Italy					■						■	
Saudi Arabia					■	■						
South Africa	▫								▫			
South Korea	■				■	■					■	
Spain	■											
Turkey	■				■							

■ Yes ▫ Partly/Yes or No with exceptions/Other
No or N/A (information not available, no exxample identified)

MED = medicines, MD = medical devices

Source: GÖ FP survey

3.1.2.1 Inclusion in reimbursement list(s) despite limited evidence

(Added) therapeutic benefit is a key criterion in the reimbursement (and pricing) decisions (cf. Figure 1.4). However, even if evidence is not proven or is limited, countries have developed approaches to allow for the inclusion of defined health technologies in reimbursement (cf. Table 3.3).

Table 3.3:
Results – Examples of specific reimbursement policies: inclusion in reimbursement list(s) despite limited evidence

Specific reimbursement policies	Inclusion in reimbursement list(s) despite limited evidence/ therapeutic benefits	
	Medicines	*Medical devices*
Australia	**Yes** (for orphan medicines upon compliance with certain criteria, no CEA required)	–
Brazil	**Partly** (shortened HTA process possible)	**Partly** (reimbursement decision without assessment in case low risk medical devices
France	**Yes** (no HTA for medicines included in the DRG system)	–
Germany	**Yes** (e.g. orphan medicines, novel antibiotics effective in AMR and low-budget medicines are exempt from the need to have to provide an additional therapeutic benefit)	**Yes** (e.g. new innovative medical devices are exempt from the evaluation of the added therapeutic benefit, initiation of a government sponsored trial to demonstrate the benefit of a new medical device in case of insufficient evidence)
Italy	–	–
Saudi Arabia	–	–
South Africa	**Exceptionally** (request for reimbursement for medicines excluded from the Essential Medicines List (EML) possible in exceptional circumstances for specific patients)	–
South Korea	**Yes** (certain cancer medicines and orphan medicines, for which evidence of cost-effectiveness or significant improvement in clinical outcomes cannot be produced, may be exempt from CEA under specific conditions; designated essential medicines always exempt)	–
Spain	**Yes** (decision on inclusion in hospital budgets (i.e. DRG funding) not based on an HTA in inpatient sector)	–
Turkey	**Yes** (no pharmaco-economic evidence required for orphan medicines and generics with originator in positive list as prerequisite for inclusion in the reimbursement list)	–

CEA = cost-effectiveness analysis, DRG = diagnosis-related group, HTA = Health Technology Assessment

Source: GÖ FP survey

A common feature is to lower the evidence requirements and to waive defined health technologies from those assessments (e.g. cost-effectiveness analysis, pharmacoeconomic evaluation) that are

usually done on a routine basis in the reimbursement process.[15] They include waivers from cost-effectiveness analysis (Australia, South Korea), pharmaco-economic evaluation (Turkey) or "early benefit assessment" (name for the HTA process in Germany). Orphan medicines are among the group of medicines for which such waivers are most frequently applied (Australia, Germany, South Korea and Turkey). Germany and South Korea have a waiver for further medicines (cf. Box 3.1 and Box 3.3). The South Korean example is shown in more detail (Box 3.1, Box 3.2 and Figure 3.4) as it highlights the interlinkage of pricing and reimbursement decision processes.

Box 3.1:
Results – Cost-effectiveness analysis in pricing and reimbursement in South Korea

South Korea – Pricing and Reimbursement for new medicines (cf. Figure 3.4).

When a new medicine is evaluated for reimbursement and alternative medicines are already available, the clinical effectiveness of the new medicine is compared to its alternative(s). If the clinical effectiveness of the new medicine is found to be non-inferior compared to alternative(s), the price of the new medicine is, in principle, negotiated below the weighted (by volume) average price of the reimbursed alternatives. However, a price negotiation is not required, if the manufacturer accepts the price of its new medicine to be between 90-100% of the weighted average price of the alternatives. The amount of percentage reduction depends on the type of medicine:

- new biological and orphan medicines do not require price negotiation if the proposed prices is equal to or below the weighted average price of alternatives,
- paediatric medicines are exempted from price negotiations if the manufacturer proposes a price equal to or below 95% of the weighted average price of alternatives.
- For other medicines, no negotiation is required if the proposed price does not exceed 90% of the weighted average price of alternatives

For medicines with superior clinical effectiveness compared to their alternatives, the price is determined based on a cost-effectiveness evaluation. Medicines that are found to be cost-effective can only be reimbursed after negotiations have been held and a financial agreement has been concluded between the manufacturer and the NHIS.

Medicines that are found to be inferior to their alternatives are not considered for reimbursement. New medicines for which no alternatives are available and which are classified as essential for treatment by the Drug Benefit Coverage Assessment Committee (DBCAC) of the Health Insurance Review and Assessment Service (HIRA) are not required to submit a cost-effectiveness evaluation (cf. also Box 3.2). In this case, the NHIS negotiates the prices with the manufacturers based on the prices in seven other countries (with a focus on U.S., Japan, Great Britain, France, Germany, Switzerland, and Italy; although selected countries may vary).

Source: GÖ FP survey

[15] These HTA as part of pricing and reimbursement decisions are on top of the evaluations on safety, effectiveness and quality in the decision process of the regulatory authority on marketing authorisation.

Germany is an interesting example as it grants these exemptions for antibiotics and – as the only case study country – also for medical devices, namely in the context of AMR (cf. Box 3.3). In some countries (Germany, France, Spain), the decision on inclusion in hospital budgets (i.e. DRG funding) is not based on an HTA (inpatient sector).

Box 3.2:
Results – Exemptions from submitting an economic evaluation for reimbursement assessment in South Korea

South Korea – Cost-effectiveness analysis waiver system

For certain cancer or orphan medicines for which evidence of cost-effectiveness may be difficult to produce, the manufacturer may choose to be exempted from providing an economic evaluation report for the reimbursement assessment (instead of entering a risk-sharing agreement for which it would have to submit an economic evaluation). In this case, the ex-factory price plus the distribution margin and VAT of the medicine in at least three of seven countries (i.e. U.S., Japan, United Kingdom, France, Germany, Switzerland, and Italy; countries to be considered may vary) is used as benchmark for negotiations. All new medicines that make use of this system are required to reach an expenditure cap with the NHIS.

South Korea – Designated as essential medicines

A cost-effectiveness analysis is not required for medicines designated by the DBCAC of HIRA as essential for treatment. The medicine's reimbursement price is then determined by negotiation between the manufacturer and the NHIS based on the price of the medicine in seven countries (i.e. U.S., Japan, United Kingdom, France, Germany, Switzerland, and Italy; selected countries may vary). In order to be designated essential, medicines are required to meet all of the following criteria:

- Medicines for which no alternative therapies are available
- Medicines that are used for life-threatening diseases
- Medicines that are used to treat small groups of patients, such as those with rare diseases
- Medicines that are proven to provide significant improvements in clinical efficacy or survival

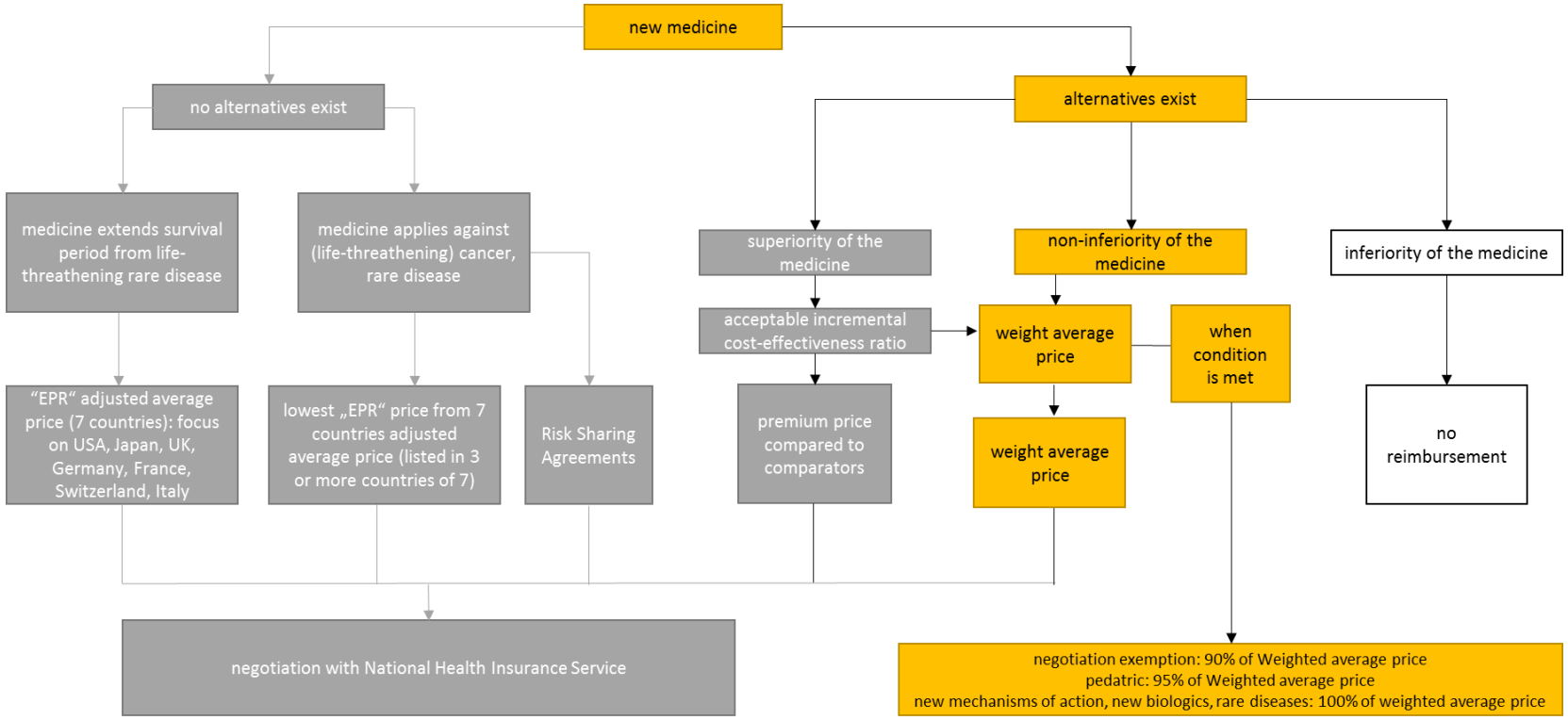
In addition, other medicines deemed essential by the DBCAC can be designated as essential medicines.

South Korea – Lower reimbursement price

A manufacturer that applies for a medicine with a lower reimbursement price than the one for existing alternatives in the NHIS positive list can be exempted from submitting an economic evaluation report.

Source: GÖ FP survey

Figure 3.4:
Results – Evaluation process for pricing and reimbursement of new medicines in South Korea



Source: GÖ FP based on Yoo et al. 2019 [104]

Box 3.3:
Results – Exemptions from the need for proof of additional benefit in Germany

Germany – Exemption from HTA for defined antibiotics and some other medicines

Orphan medicines and medicines of low economic impact

For orphan medicines, the additional therapeutic benefit is assumed based on their marketing authorisation, but the extent of the benefit is assessed. If orphan medicines have a higher economic impact than € 50 million, a normal benefit assessment will be conducted.

Medicines of little economic impact (below annual turnover of €1 million with statutory health insurance) are exempt from the "early benefit assessment".

Update for 2021 – Exemptions from HTA for reserve antibiotics

Based on legislation as of March 2020, from 2021 onwards, the HTA procedure for so-called "reserve antibiotics" against multi-resistant bacteria will be designed similarly to the regulation foreseen for orphan medicines. If a new antibiotic is effective against infections caused by multi-resistant bacterial pathogens for which only limited alternative therapy options are available, it is exempt from the need to prove its additional benefit (i.e. exemption from HTA).

At the time of writing, the procedure for reserve antibiotics was being developed. The Robert Koch Institute (RKI), has to determine, in agreement with the Federal Institute for Drugs and Medical Devices (BfArM), the criteria for classifying an antibiotic as a reserve antibiotic until 31 December 2020. If a new antibiotic does not meet the criteria defined by the RKI, a normal "early benefit assessment" will be conducted, and AMR will also have to be taken into account.

In anticipation, already in September 2020, the benefit assessment for a potential reserve antibiotic (ceftolozane/tazobactam) was discontinued by the G-BA for all four areas of application (hospital-acquired pneumonia, complicated intra-abdominal infections, complicated urinary tract infections or acute inflammations of renal pelvis). In 2021, it will be decided whether or not ceftolozane/tazobactam is to be classified as a reserve antibiotic (IQWIG did not find any proofs of superiority or additional benefit for ceftolozan/Tazobactam).

Government-sponsored trials for medical devices with limited evidence

If a new medical device fails to demonstrate its benefits, but would be of interest for the health system, a government-sponsored trial can be launched.

Source: GÖ FP survey and literature [105]

In a broader sense, the exceptional reimbursement of medicines not included in the Essential Medicines List (EML) for defined patients in South Africa could also be considered as an exemption classified under this category.

3.1.2.2 Higher reimbursement rates

In those countries where differentiated reimbursement rates for outpatient medicines are applied (some groups of medicines receive a higher reimbursement rate), this mechanism could be used to privilege specific medicines and thus also protect patients from co-payments. This approach is applied for severe and chronic diseases in France (cf. Box 3.4).

Box 3.4:
Results – Exemptions from co-payments for medicines and medical devices for chronic diseases in France

France – Exemption from co-payments

Medicines

France applies different percentage reimbursement rates for outpatient medicines funded by Social Insurance depending on the assessed "medical value" (65%, 30%, 15%). As a result, patients co-pay percentage co-payments of 35%, 70% and 85%, depending on the reimbursement rate. These co-payments are usually reimbursed by their "mutuelle" insurance. In addition, adults above 18 years are charged a prescription fee of € 0.50 for each medicine pack (exemption for children), up to an annual cap of € 50 spent by patients on the prescription fee.

Medicines to treat severe and chronic diseases (Affections de longue durée / ALD) are always 100% reimbursed (around 30 diseases listed in this long duration diseases list).

Medical devices

The ADL scheme is also applicable for medical devices: Patients with defined severe and chronic diseases under the ALD schemes are also exempt from co-payments for medical devices related to these diseases. For medical devices used in the outpatient sector, a co-payment of 40% is, in principle, applicable, which is, in practice, again covered by the complementary health insurance ("mutuelle").

Source: GÖ FP survey

3.1.2.3 Faster access into reimbursement

In seven of the ten study countries approaches allowing faster market access were identified (for medicines, and thereof in three countries for medical devices). In some countries (e.g. Italy, South Korea), procedures in the reimbursement decision-making process (negotiation time) are shortened for defined medicines such as innovative medicines or orphan medicines. Some countries have explicit early access schemes (cf. Table 3.4).

Australia, France (cf. Box 3.5) and Italy are countries with defined early access schemes which also allow early use of defined health technologies (medicines and also medical devices in some cases) at the expense of the public payers.

Table 3.4:
Results – Examples of specific reimbursement policies: faster access in reimbursement

Specific reimbursement policies	Faster access in reimbursement (e.g. early access schemes)	
	Medicines	*Medical devices*
Australia	**Yes** (special access scheme, priority review and provisional approval pathway; clinical trial schemes (exemption or notification schemes for early patient access))	–
Brazil	–	–
France	**Yes** (early access scheme ATU)	**Yes** (temporary funding of innovative MD through a dedicated exceptional pathway)
Germany	**Yes** (automatic reimbursement at a price the manufacturer freely sets)	–
Italy	**Yes** (early access schemes (e.g. compassionate use, AIFA 5% fund); fast-track negotiation for orphan medicines and medicines of special therapeutic and social relevance and hospital medicines)	–
Saudi Arabia	**Yes** (if a medicine is approved by EMA or FDA, it will enter the fast track registration)	**Yes** (access to innovative MD may be accelerated, if supplier can comply with certain criteria)
South Africa	–	–
South Korea	**Yes** (innovative new medicines, approved first in South Korea, clinical trials conducted in South Korea, developed by R&D-oriented pharmaceutical company, are subject to shorter reimbursement assessment period and price negotiation period; certain innovative medicines can be subjected to expedited review, e.g. medicines to treat life-threatening diseases such as cancers; medicines that require urgent introduction)	**Yes** (for new procedures: to shorten the period under market entry MoHW implemented Parallel Review Process for simultaneous review in the regulatory application and the new HTA application)
Spain	–	–
Turkey	**Yes** (special access schemes e.g. Named Patient Programme, compassionate use)	–

AIFA = Agenzia Italiana del Farmaco / Italian Medicines Agency, ATU = Authorisation temporaire d'utilisation, EMA = European Medicines Agency, FDA = Federal Drug Agency, HTA = Health Technology Assessment, MoHW = Ministry of Health and Welfare, R&D = research and development

Source: GÖ FP survey

While not officially called an early access scheme, the German reimbursement system could be considered as such [106]. As in the South Korean example above (cf. Figure 3.4), reimbursement and pricing policies are closely interlinked, so that a description of solely pricing or solely reimbursement would be too narrow. The design of this specific reimbursement and pricing policy in Germany will thus be displayed in chapter 3.2.2.1 on pricing policies.

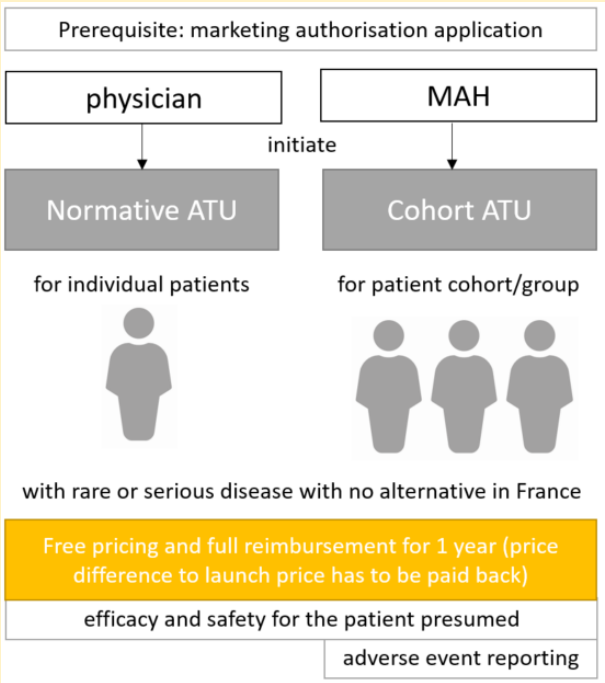
Box 3.5:
Results – Early access scheme in France

France: ATU for medicines

France has an early access scheme called "Autorisation temporaire d'utilisation" (ATU). It is in place for medicines that are intended to treat serious or rare diseases, in the absence of appropriate treatment and when the treatment cannot be postponed.

Free pricing is in place (i.e. the manufacturer can freely set the price at a level it considers "value"). Once the medicine obtains marketing authorisation, an HTA is performed. Based on the results of the HTA, the price negotiation between the Pricing Committee CEPS and the manufacturer takes place.

Should the negotiated price be lower than the free set price under the ATU, the manufacturer has to pay back the difference (so-called "post-ATU" discounts).



Currently, for instance, the antiviral bulevirtide 2mg (powder pour injectable solution) by Myr has been included in the ATU (since 9 September 2019). No antibiotic is, for the time being, in the ATU.

"Forfait innovation"

The "forfait innovation" is a kind of ATU for **innovative medical devices and processes. It offers temporary partial or full funding.**

Source: GÖ FP survey and [107] for integrated figure

3.1.2.4 Omitting reimbursement reviews

In some countries, legislation provides for regular reviews of (specific) medicines at defined periods in time. The review aims to assess if reimbursable medicines continue to comply with the criteria to remain on the reimbursement list or if they should be delisted. Such a reimbursement review could be waived to ensure longer reimbursement over time even if criteria might no longer be applicable. No example from any of the countries was reported to omit regularly planned reimbursement reviews to incentivize specific medicines. However, the French additional list ("liste en sus", see below chapter 3.1.2.6), used in hospitals to provide additional funding on top of DRG funding, could still be of interest in this context. The idea would be that expensive or low-volume

medicines on this additional list would move back to the DRG system after some time (years), with the aim that instead other medicines could get listed. However, in reality, this rarely happens: Medicines continue staying on the "additional list" which has been growing significantly.

3.1.2.5 Waiving reimbursement restrictions / conditions of use

Public payers tend to link (and limit) reimbursement of medicines to specific (prescribing) guidelines or conditions of use to support more clinically approved use, as with regard to antibiotics (cf. Box 3.6). Exemptions may be allowed, and this may be supportive to patients, prescribers and marketing authorisation holders and suppliers. Australia has defined a maximum quantity and number of repeats for the top 5 prescribed medicines in the outpatient sector (cf. Box 3.6), for clinical reasons. In addition, there has been an exception, namely allowing hospitals to prescribe and dispense the maximum amount of an antibiotic on discharge to ensure proper antimicrobial use. In Germany, laboratory diagnostics for antibiotic therapy are exempt from the so-called "profitability control"; thus, prescribers can use and prescribe them in unlimited number without having to substantiate use.

Box 3.6:
Results – Repeat antibiotics filling under defined conditions in Australia

National AMR Strategy in Australia: Revised PBS listings for antibiotics

There is a maximum quantity and number of repetitively prescribing the following antibiotics in the Pharmaceutical Benefits Scheme (PBS): amoxicilline, amoxicilline with clavulanic acid, cefalexine, doxycycline and roxithromycin. Patients must meet the restriction criteria for the PBS listed antibiotics, and prescribers must prescribe quantities and repeats of antibiotics in line with current therapeutic guidelines. These restrictions are intended to encourage clinicians to only prescribe an antibiotic repetitively when clinically indicated.

Background: In 2018, the Australian Department of Health reviewed PBS listings of frequently used antibiotics that allowed repeat prescriptions to be issued as the default setting for computer-generated prescriptions. The aim of this review was to reduce antibiotic prescribing without impacting clinical decision making, by ensuring that health professionals could actively decide to prescribe repeats for antibiotics where clinically indicated. The antibiotics selected were the top five dispensed antibiotics on the PBS, which represented over 70% of all dispensed antibiotics under the PBS in 2017.

Outpatient hospital supplies

The Pharmaceutical Reform Agreements (PRA) permit approved public hospitals to prescribe and dispense medicines up to the PBS maximum quantity on discharge, providing a smoother transition from hospital into the community setting. This has assisted in appropriate antimicrobial use since prior to the PRA, patients could only access 2–7 days of non-PBS medicines on discharge (this may not have covered the appropriate antibiotic course duration).

Source: GÖ FP survey

3.1.2.6 Add-on funding

Some countries provide separate funding for defined medicines, through ear-marked funds for specific indications or diseases or innovative medicines in general, and through separate (additional) funding mechanisms in hospitals (cf. Table 3.5). In the study countries, the latter can be found in France and in Germany (for both medicines and medical devices in both countries). Health technologies on these lists are not included in the DRG system, which is the common funding mechanism in hospitals, but they are funded individually (for details cf. Box 3.7).

Box 3.7:
Results – Add-on funding in hospitals in France and Germany

France – Add-on funding for medicines in hospitals

In France, two lists offering additional funding of medicines used in hospitals are applied: The "additional list" ("liste en sus") includes mainly high-priced and low volume medicines of "important" medical value which are mainly used in hospitals. The original idea was that medicines on this list would move back to DRG after some time but this rarely happens in practice. The "liste en sus" is also applicable for medical devices.

A second list ("rétrocession") contains medicines with limitations in supply, dispensing or administration or which require prescription and delivery monitoring. Included medicines comprise medicines derived from blood, ARV, chronic hepatitis B or C medicines, antibiotics, antifunghals, orphan medicines and cancer medicines. These medicines can also be dispensed in community pharmacies.

Around 60% of medicines used in French hospitals are either on the "liste en sus" or on the "retrocession" list.

Germany – Add-on funding in hospitals

Hospitals can obtain additional funding on top of DRG payments for new technologies, including medicines, if they have not been included in the DRG system under the new diagnostic and treatment methods regulation ("Neue Untersuchungs- und Behandlungsmethoden" / NUB).

Background: The NUB regulation was introduced by the law on hospital remuneration (Krankenhausentgeltgesetz – KHEntgG) in 2005 to overcome a disincentive for hospitals, resulting from the time lag that could keep hospitals from introducing a beneficial new technology that is more expensive than existing treatments. In Germany, the reimbursement and pricing of innovative inpatient medicines (and devices) is managed through the NUB application process. These applications are submitted by the hospitals and are approved or rejected by the Institute for the Hospital Remuneration System (InEK).

Source: GÖ FP survey

Table 3.5:
Results – Examples of specific reimbursement policies: add-on funding

Specific reimbursement policies	Add-on funding (budgets)	
	Medicines	*Medical devices*
Australia	**No**	**Yes** (e.g. specific temporary funding mechanism for innovative medical devices or procedures, offering partial or full funding for "innovation")
Brazil	**No**	**No**
France	**Yes** (additional list ("liste en sus") for new high-priced medicines and low-volume medicines, and a second list ("retrocession) of medicines not included in DRG, in hospitals, funding on top of DRG)	**No**
Germany	**Yes** (outpatient: option for additional funding (+20%) of certain methods/procedures that need additional promotion ("förderungsfähiger" Bereich) (hospitals: additional funding on top of DRG for new technologies if not included in the DRG)	**Yes** (funding for PCT test out of separate budget for three years extra budget without any capping (hospitals: additional funding on top of DRG for new technologies if not included in the DRG)
Italy	**Yes** (2 "innovation funds" of € 500 mio. each per year, one for oncology medicines and one for non-oncology medicines, additional funds for orphan medicines purchases)	**No**
Saudi Arabia	**No**	**No**
South Africa	**No**	**No**
South Korea	**Yes** (compensation to manufacturers of essential medicines with low marketability, based on designation of these medicines as shortage prevention)	**No**
Spain	**No**	**No**
Turkey	**No**	**No**

DRG = diagnosis-related group, PCT = procalcitonin test
Example for Australia could not be validated

Source: GÖ FP survey

Italy introduced funds for financing defined innovative medicines (cf. Box 3.8).

Specific funding schemes are also applicable for medical devices.

Finally, the provision for essential medicines whose market launch is considered to be not attractive for companies in South Korea is another example for a fund. These medicines are then defined as shortage prevention medicines, and the manufacturers are compensated for costs of goods or receive production incentives.

Box 3.8:
Results – Funds for procuring orphan medicines and "innovation funds" in Italy

Italy – AIFA 5% Fund

Since 2003 (Legge 326/2003), AIFA maintains the "5% Fund", which is fed by 5% of the annual expenses of pharmaceutical companies' promotional activities targeted at doctors. 50% of the fund is used to fund independent research, while the other 50% is dedicated to the purchase of orphan medicines and other medicines for the treatment of serious diseases that have not yet been authorised.

Italy – Add-on funding for medicines that are considered innovative

Medicines that qualified as innovative medicines are funded out of one of two dedicated innovation funds that were introduced in 2017. There is one fund for innovative oncology medicines and the other fund is for innovative non-oncology medicines. Each of the funds has been allocated € 500 million per year.

Medicines classified as innovative according to these criteria enjoy some benefits:

- Separate funding out of these funds
- Immediate access to the regional markets
- No application of the mandatory discount of the manufacturer to the SSN (cf. chapter 3.3.2.2)

According to Determinazione 1535/2017, there are three criteria to define the innovativeness of a medicine:

1) Unmet medical need

2) Added therapeutic benefit

3) Quality of evidence (robustness of clinical studies) which is assessed through the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) methodology

Unmet therapeutic needs	Added therapeutic value	Quality of evidence	Innovation status
MAXIMUM	MAXIMUM	HIGH	INNOVATIVE
IMPORTANT	IMPORTANT	HIGH	
MODERATE	MODERATE	MODERATE	CONDITIONALLY INNOVATIVE
POOR	POOR	LOW	NOT INNOVATIVE
ABSENT	ABSENT	VERY LOW	

There is no formal link between the innovation evaluation and the price and reimbursement negotiations.

Source: GÖ FP survey and [108] for included figure

3.2 Pricing policies in the study countries

Pricing relates to the action of a government authority to set the price of a health technology and/or indirectly influence it. In principle, there are two possibilities. Governments may apply full **price control** (i.e. regulate the price of a health technology), or they may allow the supplier to freely set the price (so-called **free pricing**). Between these two possibilities, negotiation can play an important role. Different criteria may be applied to determine a price of the technology. These include prices of the same or similar health technology in the same or other countries, the therapeutic value (e.g. the added therapeutic benefit compared to a comparator, the possibility to address unmet need), costs (e.g. production costs, research and development costs) and specific conditions. Different pricing polices may be applied for different groups of health technologies.

It should be noted that there is an overlap between pricing and procurement, since the pricing policies of price negotiations and tendering can also be considered as purchase (procurement) options.[16]

Rewards, privileges and incentives to private actors such as marketing authorisation holders and suppliers include any policy options which allow higher leverage to the price actors (such as free pricing, less price regulation) and/or higher prices (see also Figure 3.5). Five specific policies are presented as follows:

» To **grant a higher price** for a health technology that is able to make an important contribution to tackle AMR (even despite limited evidence) or to grant a **high(er) profit margin** to the supplier:
this includes to **grant** higher margins to actors in the supply chain (e.g. wholesalers, pharmacies), including exemption from or laxer regulation on **"kick-backs"** (e.g. discounts, rebates) to other private actors and to patients,

» To allow **free pricing** for an AMR-related health technology (even despite limited evidence), which will likely lead to a higher price than a regulated one,

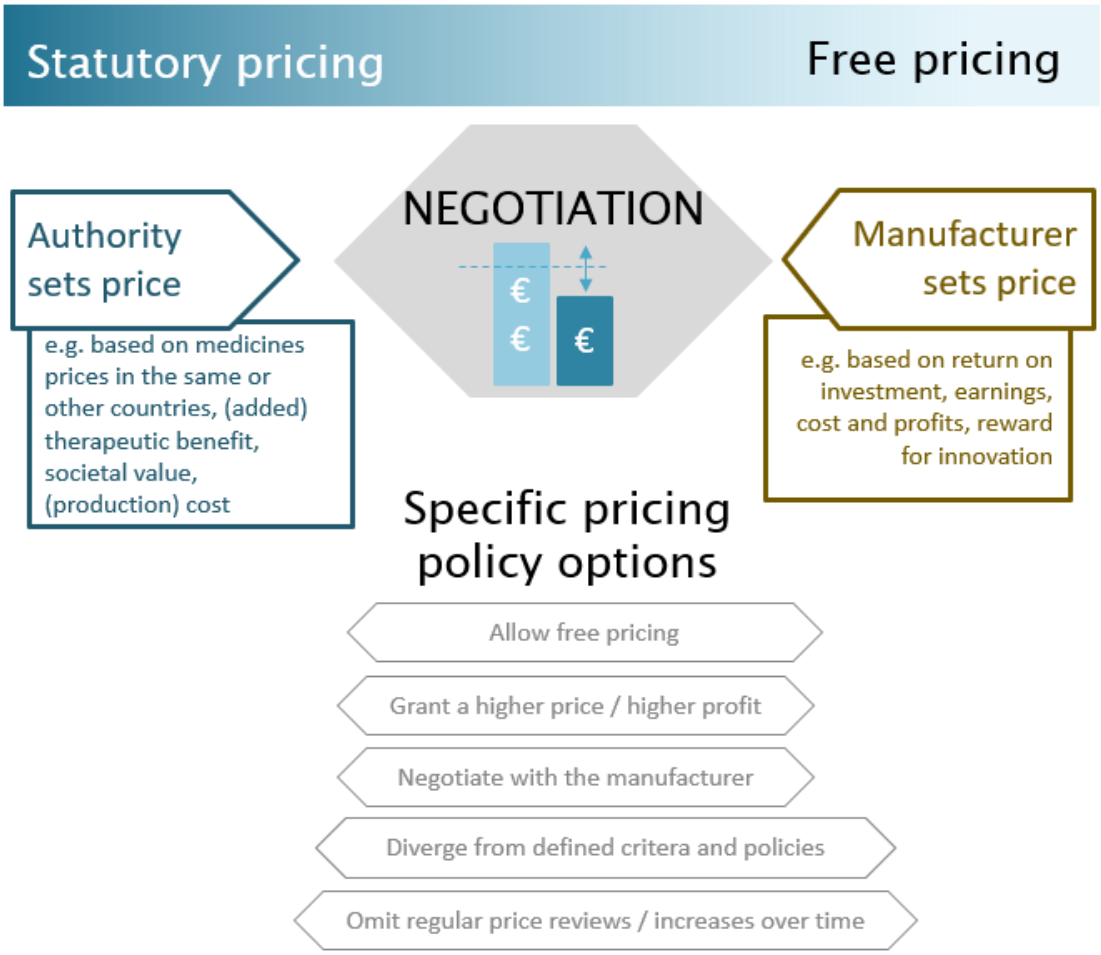
» To **negotiate** with the supplier on the price of a health technology instead of statutorily setting the price according to defined criteria (higher flexibility),

» To **diverge from defined criteria and policies** (e.g. consider the benchmark price based on external price referencing as a starting point but possibly allow a higher price; not to use pricing policy such as tenders with known cost-containment impact), and

» To **omit regular price reviews** that might result in lower prices and to allow **price increases.**

[16] Some pricing policy aspects in the wider sense (e.g. mandatory discounts and claw-back to public payers, specific policies such as tendering or MEA) will be discussed in the next chapter on procurement policy (cf. chapter 3.3.2).

Figure 3.5:
Results – Pricing policy framework and taxonomy of specific pricing policies



Source and presentation: GÖ FP

3.2.1 Standard pricing policies

As shown in Table 3.6, the prices of some or all of the medicines are regulated in all study countries, whereas for medical devices indirect price regulation through procurement is common and direct pricing policies are applied in only four countries (Australia, France, South Korea and Spain). However, there are some important specificities:

» **Price regulation** usually only **targets** those medicines which are funded (or co-funded) by public payers (these are medicines in the public sector in Brazil and South Africa and **reimbursable medicines** in the other case study countries). Only Saudi Arabia and Turkey have price regulation for all medicines.

» In four countries (Australia, France, South Korea and Spain), **some reimbursable medical devices** are also **price-regulated**.

» For all other medical devices, no direct price regulation is exercised by the public authority but **prices are indirectly determined through public procurement**. Even for price-regulated health technologies (medicines and medical devices) the final (procurement) price can change in a later stage during procurement.

» An important exemption in price regulation is Germany which allows free pricing for medicines in the first year, while the price decided by the MAH is funded by the state (cf. chapter 3.2.2.1).

» With regard to the **methodology to set the price** (pricing policy), external price referencing, internal price referencing and value-based pricing are commonly applied pricing policies.

» In contrast, **cost-plus pricing** is not in place for medical devices and **rarely** used for medicines (three countries: South Korea and – only exceptionally – Australia and South Africa). A few further countries consider production costs as background information.

» **For health technologies with competitors** on the market, **internal price referencing** (i.e. price setting based on the consideration of prices of similar health technologies in the country's market) is the major pricing policy (for medicines in all ten case study countries and for medical devices in five countries).

» New health technologies entering national markets are usually priced based on the application of **external price referencing** (i.e. price setting by consideration of the prices of that technology in other countries) in the first place (for medicines in all ten case study countries and for medical devices in two countries). A **value-based pricing** process, e.g. through a price negotiation (probably resulting a managed-entry agreement) follows, usually as a second step (for medicines in all ten case study countries, and for medical devices in two countries).

» For health technologies used in the outpatient sector, their prices may change as they move along through the supply chain. To protect patients and health systems from excessive prices, prices in the supply chain (wholesale prices, pharmacy retail prices) may be statutorily controlled through **regulation of distribution mark-ups**. This is the case for medicines in all ten case study countries, whereas it is not used in any of the four countries (Australia, France, South Korea and Spain) which have price regulation for medical devices.[17] In the hospital sector, only the ex-factory price (hospital list) is applied; in cases of procurement of health technologies (medicines and medical devices) the "procurement price" (tender price) is the sole price type of relevance, and no further price types of the supply chain come into play.

[17] The focus of this study is on policy options for the "first price type regulated" since incentives targeted at MAH and suppliers are explored. However, possibly interesting and incentivizing examples applicable in the supply chain will also be mentioned (cf. chapter 3.2.2.3).

Table 3.6:
Results – Standard pricing policies for health technologies of the study countries, 2020

Standard pricing policies		Price control (price regulation) – scope				Pricing policies							
		Price control (scope of price-regulated HT)		All price types regulated		External price referencing (EPR)		Internal price referencing (IPR)		Value-based pricing (VBP)		Cost-plus pricing	
		medicines	*medical devices*	*medicines*	*medical devices*	*medicines*	*medical devices*	*medicines*	*medical devices*	*medicines*	*medical devices*	*medicines*	*medical devices*
Australia	outpatient	**Yes** (reimbursable medicines)	**Yes** (reimbursable MD)	**Yes** (ex-factory, PPP & PRP)	No (ex-factory)	**Yes** (supportive policy)	**Yes** (supportive policy)	**Yes** (for comparable medicines)	**Yes** (for comparable MD)	**Yes** (components used for pricing decision)	**Yes** (components used for pricing decision)	**Exceptionally** (production costs uesed if no therap. alternative)	**No**
	inpatient	**No, but** (indirectly via procurement)	**No, but** (indirectly via procurement)	**Not appl.** (indirectly via procurement: procurement price	**Not appl.** (indirectly via procurement: procurement price)	**No**	**No**	**No**	**No**	**No**	**No**	**No**	**No**
Brazil	outpatient	**Yes** (all medicines in the public sector)	**No, but** (indirectly via procurement)	**Yes** (ex-factory, PPP & PRP)	**Not appl.** (indirectly via procurement: procurement price)	**Yes** (for new medicines with therapeutic benefit)	**No**	**Yes** (for generics & comparable medicines)	**No**	**Yes** (for new medicines)	**No**	**No**	**No**
	inpatient			**Yes** (ex-factory)									
France	outpatient	**Yes** (reimbursable medicines)	**Yes** (reimbursable MD)	**Yes** (ex-factory, PPP & PRP)	No (ex-factory)	**Yes** (supportive policy)	**Yes** (supportive policy)	**Yes** (for generics & biosimilars)	**Yes** (supportive policy in price negotiations)	**Yes** (for new medicines based on HTA)	**Yes** (based on assessment)	**No** (production costs as informative element in exceptional cases)	**No**
	inpatient			**Yes** (ex-factory)									
Germany	outpatient	**Yes** (reimbursable medicines from 2nd year on)	**No, but** (indirectly via procurement; price regulation for some medical aids)	**Yes** (ex-factory, PPP & PRP)	**Not appl.** (indirectly via procurement: procurement price)	**Yes** (supportive policy)	**No**	**No**	**No** (except for some medical aids)	**Yes** (for new medicines)	**No**	**No**	**No**
	inpatient			**Yes** (ex-factory)		**No**			**No**				
Italy	outpatient	**Yes** (reimbursable medicines)		**Yes** (ex-factory, PPP & PRP)	**Not appl.** (indirectly via procurement: procurement price)	**Yes** (supportive policy)	**No**	**Yes** (for generics & biosimilars)	**No** (previous use on pilot basis)	**Yes** (for new medicines, component used for pricing decision)	**No**	**No** (production costs used as informative element)	**No**
	inpatient			**Yes** (ex-factory)									
Saudi Arabia	outpatient	**Yes** (all medicines)	**No, but** (indirectly via procurement)	**Yes** (ex-factory, PPP & PRP)	**Not appl.** (indirectly via procurement: procurement price)	**Yes** (for all new medicines)	**No**	**Yes** (as benchmark, not implemented by law)	**No**	**Yes** (therapeutic significance & pharmacoeconomic studies have influence)	**No**	**Exceptionally** (not systematically)	**No**
	inpatient			**Yes** (ex-factory)									

Standard pricing policies		Price control (price regulation) – scope				Pricing policies							
		Price control (scope of price-regulated HT)		All price types regulated		External price referencing (EPR)		Internal price referencing (IPR)		Value-based pricing (VBP)		Cost-plus pricing	
		medicines	*medical devices*	*medicines*	*medical devices*	*medicines*	*medical devices*	*medicines*	*medical devices*	*medicines*	*medical devices*	*medicines*	*medical devices*
South Africa	outpatient	**Yes** (on-patent medicines in public sector)	**No, but** (indirectly via procurement)	**Yes** (ex-factory, PPP & PRP)	**Not appl.** (indirectly via procurement: procurement price)	**Yes** (supportive policy in public sector)	**No**	**Yes** (for generics)	**No**	**Yes** (but not routinely)	**No**	**Exceptionally** (not for scheduled or prescription medicines)	**No**
	inpatient			**Yes** (ex-factory)									
South Korea	outpatient	**Yes** (reimbursable medicines)	**Yes** (reimbursable MD)	**Yes** (ex-factory, PPP & PRP)	No (ex-factory)	**Yes** (supportive policy)	**N/A**	**Yes** (for generics & biosimilars)	**Partly** (i.e. MD in same functional category)	**Yes** (for new medicines, economic evaluation)	**Yes** (value appraisal standards)	**Yes**	**N/A**
	inpatient												
Spain	outpatient	**Yes** (reimbursable medicines)	**Yes** (reimbursable MD - no Dx)	**Yes** (ex-factory, PPP & PRP)	**Yes** (ex-factory/tender)	**Yes** (supplementary policy)	**No**	**Yes** (for generics & biosimilars)	**Yes** (for reimbursable MD)	**Yes** (based on HTA)	**No**	**No** (production costs used as informative element)	**No**
	inpatient		**No, but** (indirectly via procurement; price regulation for some medical aids)	**Yes** (ex-factory)	**Not appl.** (indirectly via procurement: procurement price)								
Turkey	outpatient	**Yes** (all medicines)	**No, but** (indirectly via procurement)	**Yes** (ex-factory, PPP & PRP)	**Not appl.** (indirectly via procurement: procurement price)	**Yes** (key policy)	**No**	**Yes** (for generics)	**No**	**Yes** (based on added therapeutic benefit & pharmacoeconomic assessment)	**N/A**	**No**	**No**
	inpatient			**Yes** (ex-factory)				**No**					

EPR = external price referencing, ex-factory = ex-factory price (manufacturer price), HT = health technology, IPR = internal price referencing, MD = medical device(s), PPP = pharmacy purchasing price (wholesale price), PRP = pharmacy retail price, VBP = value-based pricing
Presented pricing policies (such as EPR, IPR) relate to the "first price type regulated", i.e. the ex-factory price in the study case countries. Information on price regulation for other price types such as PPP or PRP is presented in the column entitled "all price types regulated".
Procurement policies may be used, either in addition to a direct pricing policies (e.g. EPR) or instead of a direct pricing policy. Procurement-related policies (e.g. tendering, managed-entry agreements and collaborative policies) are addressed in chapter 3.3.

Source: GÖ FP survey

For the study countries, standard and specific pricing policies are shown in country-specific flow-charts in chapter 7.2 in the Annex.

3.2.2 Specific pricing policies in the study countries

In the case study countries, governments apply specific pricing policies, or a specific design in their pricing policies, to incentivize the market entry of (needed) health technologies. Table 3.7 provides an overview, and details are presented in the following sub-chapters.

Table 3.7:
Results – Overview of specific pricing policies for health technologies of the study countries, 2020

Specific reimbursement policies for defined health technologies	Free pricing (no direct price regulation)[1]		Price negotiations		Higher prices / higher profits[2]		Diverging from pricing policies / criteria		Omitting price reviews / increases over time	
	MED	MD	MED	MD	MED	MD	MED	MD	MED	MD
Australia										
Brazil										
France										
Germany										
Italy										
Saudi Arabia										
South Africa										
South Korea										
Spain										
Turkey										

Yes | Partly / Yes or No with exceptions

No or N/A (i.e. no information available, no specific examples identified)

[1] Indirect price regulation through procurement based on different methods (e.g. tendering, open procedure, direct negotiation, framework agreements) may still be applied.
[2] E.g. granting "premium prices"
Some policies are overlapping
Information relates to outpatient and inpatient sectors unless specified differently.

Source: GÖ FP survey

3.2.2.1 Free pricing

A major incentive to market entry is to allow MAH and suppliers to set the price of health technologies at their own discretion, without any restrictions or applying of criteria (free pricing).

In most case study countries, MAH are allowed to freely set the price of those medicines that are not funded by the public payer or state (medicines in the private sector or in the non-reimbursement market; cf. Table 3.8). Exemptions Saudi Arabia and Turkey fix the prices of all medicines independent of their reimbursement status. A similar free pricing situation applies for non-reimbursable medical devices in four case study countries (Australia, France, South Korea and Spain) where only reimbursable medical devices are subject to price control (few medical devices are reimbursed in France and Spain, some in Australia and most medical devices in South Korea).

However, if health technologies are procured by the public sector, then there is indirect price control. So no specific incentive is provided to the MAH or supplier. Procurement activities are commonly in place for medicines used in hospitals (not explicitly visible in Table 3.8) and for outpatient and inpatient medical devices in all case study countries.

Table 3.8:
Results – Examples of specific pricing policies: free pricing

Specific pricing policies	Free pricing for defined health technologies (unless indirect price control via procurement)	
	Medicines	*Medical devices*
Australia	**Yes** for non-reimbursable med.	**Yes** for non-reimbursable MD
Brazil	**Yes** for med. in the private sector	**Yes** for all MD
France	**Yes** for non-reimbursable med.	**Yes** for non-reimbursable MD
Germany	**Yes** for all outpatient med. in the first 12 months, from 2nd year on: for all non-reimb. med.	**Yes** for all MD
Italy	**Yes** for non-reimbursable med.	**Yes** for all MD
Saudi Arabia	**No**	**Yes** for all MD
South Africa	**Yes** for med. in the private sector	**Yes** for all MD
South Korea	**Yes** for non-reimbursable med.	**Yes** for non-reimbursable MD
Spain	**Yes** for non-reimbursable med.	**Yes,** for non-reimbursable MD
Turkey	**No**	**Yes** for all MD

MD = medical devices, med. = medicines

Source: GÖ FP survey

An example for a major exemption is the specific policy and reimbursement policy approach for new medicines in Germany. All marketing authorisation holders are allowed to freely set the price of the medicine in the first year, and this price is fully covered by the public payer (cf. Box 3.9).

Box 3.9:
Results – Free pricing of reimbursable medicines in the first year in Germany

The AMNOG system in Germany

Since 2011, the "Arzneimittelmarktneuordnungsgesetz" (AMNOG) has been in place in Germany, and it substantially changed the pricing and reimbursement policy framework (before there was completely free pricing).

According to the AMNOG legislation, all new medicines are automatically reimbursed by social health insurance funds upon launch. The only exemption are those prescription-only medicines that are included in the negative list maintained by the Federal Joint Committee (Gemeinsamer Bundesausschuss / G-BA). In contrast to other countries, no criteria such as (added) therapeutic benefit, budget impact, cost-effectiveness, medical need/priority, safety or others are of relevance since medicines are considered reimbursable as soon as launched.

Medicines can immediately enter the German market after having received a marketing authorisation, and the price of the medicine is – independent from its amount – funded by the SHI. Thus, there is free pricing at launch. Prices are regulated only from the second year onwards. The price is negotiated taking into consideration the systematic and formal assessment of the "added therapeutic benefit" (so-called "early benefit assessment) of a new medicine which is performed within twelve months after market launch.

Even if the price determined through statutory pricing for the second and further years is lower than the price in the first year, there is no mechanism requiring the marketing authorisation holder to pay back the difference between the higher and lower price. Furthermore, price ceilings can be exceeded in "justified individual cases" if arbitration courts decide accordingly.

Source: GÖ FP survey and literature [106, 109]

The policy decision on whether to allow free pricing or to statutorily set the price by the pricing authority can be supplemented by possible procurement activities (e.g. tendering or price negotiations, including the conclusion of a managed-entry agreement). This is typically seen for health technologies used in hospitals and those that impact public budgets (i.e. with high prices).

3.2.2.2 Price negotiations

As explained at the beginning of this chapter, price negotiation is a pricing policy, which is allocated between statutory pricing and free pricing. Price negotiations are regularly applied in all study countries (cf. Table 3.9).

Table 3.9:
Results – Examples of specific pricing policies: price negotiations

Specific pricing policies	Price negotiations	
	Medicines	*Medical devices*
Australia	**Yes** OP: between manufacturer and Department of Health IP: between manufacturer and hospitals	**Yes** OP: between manufacturer and Department of Health IP: between manufacturer and hospitals
Brazil	**Yes** OP/IP: on national/state/district/municipality/hospital level	**Yes** OP/IP: on national/state/district/municipality/hospital level
France	**Yes** OP/IP: key approach for new reimb. med. linked to value assessment	**Yes** OP/IP: key approach for new reimb. med. linked to value assessment
Germany	**Yes** OP: between manufacturer and SHI (i.e. for generics) IP: between manufacturer and hospitals	**Yes** OP: partly (see procurement chapter) IP: between manufacturer and hospitals
Italy	**Yes** OP/IP: key approach for new med. linked to VBP	**No**
Saudi Arabia	**Yes** OP/IP: used for central procurement	**Yes** OP/IP: used for central procurement
South Africa	**Yes** OP/IP: major approach	**No**
South Korea	**Yes** OP/IP: major approach	**N/A**
Spain	**Yes** OP/IP: key approach for new med. linked to VBP, considers several components	**No**
Turkey	**Yes** OP/IP: for all med. in early/special access schemes, including Alternative Reimbursement agreements (MEA)	**Yes** OP/IP: MEA adopted on pilot basis

IP = inpatient, MEA = managed-entry agreement(s), N/A = information not available / no example identified, OP = outpatient, SHI = social health insurance

Source: GÖ FP survey

In some countries, the negotiations are linked to procurement processes at national level (done by the procurement agency), e.g. in Saudi Arabia and South Africa. Price negotiations for new, usually high-priced, medicines between a national pricing authority and the manufacturer are a common pricing policy in in Australia, France, Germany, Italy and Spain. They consider the value in addition to other pieces of information (e.g. prices in other countries) serving as supplementary background information. This is usually expressed in terms of (added) therapeutic benefit) of the health technology. For medical devices, price negotiations, as the major pricing policy between a national authority and the supplier, are less frequently performed in the study countries (e.g. conducted in France for reimbursable medical devices and in Saudi Arabia as part of national procurement).

In addition to national practices, negotiations between the supplier and a hospital (or a group of hospitals, e.g. a region or a state) are commonly performed in the study countries. This is the case for both medicines and medical devices.

For health technologies with high budget impact (i.e. high prices of single technologies or high-volume products) and/or of limited evidence of the therapeutic benefit, managed-entry agreements are commonly concluded (cf. chapter 3.3.2.1).

3.2.2.3 Higher prices and/or higher profit

For new medicines, usually value-based pricing applies to a lesser or larger extent in all study countries (cf. Table 3.10). This is guided by the principle that for higher (added) therapeutic benefit, as evidenced in an HTA, higher prices are granted. In some countries (e.g. Germany, Saudi Arabia), the term "premium price" is used. Lower requirements for HTA and exemptions from HTA (e.g. for novel antibiotics in Germany, cf. Box 3.3) support higher prices (cf. chapter 3.1.2.1).

Box 3.10:
Results – Premium prices for innovative medicines in South Korea

South Korea – innovative medicines

The price of a new innovative medicine may exceed the price of its alternatives by 10% if it meets all of the following three conditions:

- manufactured by a R&D-oriented pharmaceutical company,
- clinical trials were conducted in South Korea and
- approved in South Korea first.

The new innovative medicine's reimbursement assessment period is reduced to a maximum of 100 days (instead of 120 days), and a price negotiation period of a maximum of 30 days applies.

A "biobetter medicine" (i.e. an improved version of a known biological) can be priced at up to a 20% premium above the price of the reference medicine.

For a biosimilar, the price is set at 80% (instead of 70%) of the reference medicine's price for up to 3 years, if the clinical trials were conducted in Korea and if it is manufactured by a R&D-oriented pharmaceutical company. After three years, the price of the biosimilar is reduced to 70% of the price of the reference medicine. The price of a double-concentration biological product can be 1.9 times higher than the price of its alternative low concentration formulation.

South Korea – superior medical devices

Medical devices that have proven to be significantly superior in terms of clinical and economic outcomes compared to listed alternatives may receive a premium of up to 50%. Furthermore, suppliers of new medical devices or diagnostics may use evidence on improvements in material, shape and size to justify their application for reimbursement at the highest ceiling price.

Definition for biobetter: a biological medicine that seek superiority in one or more aspect of the clinical profile compared to an existing biological [110]

Source: GÖ FP survey

Another criterion that is taken into consideration in a few study countries to grant preferential prices is support for local production. This is the case in Saudi Africa in the procurement process (cf. Box 3.15) and in South Korea, in addition to a consideration of the therapeutic benefit (cf. Box 3.1, Box 3.10 and Figure 3.4).

Table 3.10:
Results – Examples of specific pricing policies: higher prices

Specific pricing policies	Higher prices / higher profits for defined health technologies	
	Medicines	*Medical devices*
Australia	**Yes** higher prices for medicines with added therapeutic value	**N/A**
Brazil	**Yes** exemption of several medicines from federal tax	**N/A**
France	**Yes** higher prices for medicines with added therapeutic value	**Yes** higher prices for MD with added therapeutic value
Germany	**Yes** premium prices for medicines with added therapeutic benefit price ceilings can be exceeded in "justified Individual cases" if abritation courts decide accordingly	**N/A**
Italy	**Yes** higher prices for medicines with added therapeutic value higher wholesale and pharmacy margins for generics compared to originators and biosimilars lower value-added tax rate for therapeutic oxygen than for other medicines	**N/A**
Saudi Arabia	**Yes** premium prices for medicines with added therapeutic benefit	**N/A**
South Africa	**Yes** government may be willing to pay premium prices to national medicine manufacturers; local subsidiaries of foreign multinational firms are not eligible for preferential treatment	**N/A**
South Korea	**Yes** premium prices (+10% above alternative) for new Innovative medicines specific price incentivizes for biologicals, including bioismilars locally manufactured	**Yes** premium prices (up to +50%) for MD with significant clinical and economic superiority
Spain	**Yes** higher prices for medicines with added therapeutic value	**N/A**
Turkey	**Yes** higher prices for medicines with added therapeutic value exemption from external and internal price referencing policies in some cases	**N/A**

N/A = information not available / no example identified

Source: GÖ FP survey

The example of South Korea is one of the few that was identified in the medical devices area. In France, prices of a few – reimbursable – medical devices are also price-regulated at national level, and here the added therapeutic value determines higher prices.

As stated earlier, pricing policies may also be targeted at other price components and price types (e.g. across the value chain). In Brazil, for instance, defined medicines are exempt from federal taxes. Further examples (on France and Italy) are found in Box 3.11.

Box 3.11:
Results – Higher discounts in the supply chain allowed for generics in France and Italy

France – higher discounts for generics

France regulated the commercial discount in the supply chain: Discounts which wholesalers may grant community pharmacies are capped at 2.5% for reimbursed non-generic medicines. They may be larger for reimbursed generic medicines and non-generics with prices aligned to their generic medicines, i.e. capped at 40%, thus privileging generic medicines.

Italy – higher discounts for generics

In Italy, legislation allows higher wholesale and pharmacy margins for generics compared to originators and biosimilars. The value-added tax is lower for therapeutic oxygen (10%, considered as a medicine) than for other medicines (22%).

Source: GÖ FP survey

3.2.2.4 Diverging from pricing policies and criteria

As shown in Table 3.11, specific pricing policies are applied for defined (groups of) health technologies. Exemptions are possible. In Turkey, for instance, generic versions of medicines must be priced at a certain percentage below the price of the originator. Blood products and orphan medicines are, however, exempt from the so-called price link policy. Furthermore, it neither applies for the biological market (including biosimilar medicines) nor for hospital-only medicines. A few further defined medicines (e.g. those under a named patient programme, which is an early access scheme), are exempt from pricing through external price referencing, and mandatory discounts are not applied.

It was reported from Spain that "innovation" is considered in the assessment of medicines. In practice, this mean that AMR avoiding effects of novel antibiotics can be and are considered for the price decision, even if this is not explicitly written in legislation.

Overall, only a few examples of diverging criteria could be identified in the study countries. However, this does not mean that they do not exist. In particular, price negotiations, which are concluded for new medicines and sometimes also for new medical devices (cf. chapter 3.2.2.2), are value-based and allow some flexibility.

Table 3.11:
Results – Examples of specific pricing policies: diverging from pricing policies and criteria

Specific pricing policies	Diverging from pricing policies / criteria	
	Medicines	*Medical devices*
Australia	**N/A**	**N/A**
Brazil	**N/A**	**N/A**
France	**Yes** price negotiations (VBP based) allow flexibility	**Yes** price negotiations (VBP based) allow flexibility
Germany	**Yes** price negotiations (VBP based) allow flexibility	**Yes** further negotiations of prices if they exceed existing DRG
Italy	**Yes** price negotiations (VBP based) allow flexibility	**N/A**
Saudi Arabia	**N/A**	**N/A**
South Africa	**N/A**	**N/A**
South Korea	**Yes** price negotiations (VBP based) allow flexibility	**N/A**
Spain	**Yes** price negotiations (VBP based) allow flexibility, consideration of AMR in antibiotics assessment	**N/A**
Turkey	**Yes** exemption of blood products, orphan medicines and biosimilars from the generic price link policy exemption for few further medicines (Named Patient Programme) from external price referencing and mandatory discount in exceptional cases	**N/A**

DRG = diagnosis-related groups, N/A = information not available / no example identified, VBP = value-based pricing

Source: GÖ FP survey

3.2.2.5 Omitting price reviews / allowing price increases

In none of the study countries, a specific policy was to omit regular planned price reviews, with possibly subsequent price decreases, for defined health technologies.

With regard to price increases, Australia allows manufacturers to seek price increases for defined medicines (e.g. for clinically important medicines) once per year.

3.3 Procurement policies in the study countries

Procurement relates to the process of purchasing health technologies that involves many steps and many stakeholders based on national, or supranational, regulation, policies, structures and procedures. With regard to health technologies, procurement is frequently linked to the inpatient sector when hospitals purchase health technologies.

3.3.1 Standard procurement policies

The traditional way to procure is **tendering** which is formal and competitive procurement procedure through which tenders (offers) are requested, received and evaluated for the procurement of goods or services. The tenderer with the most advantageous bid is awarded; typically this is the lowest-priced bid.

Procurement of medicines and medical devices, including AMR health technologies, through tendering is commonly done in all study countries. It is, in particular, applied for medicines and medical devices in the inpatient sector (frequently done by individual hospitals). National procurement agencies purchase – at least in part – medicines and medical devices. Table 3.12 provides an overview of standard procurement features in the study countries, supplemented by further information on specific procurement policies. In contrast to reimbursement and pricing policies, the differentiation between standard and specific procurement policies is more difficult and somewhat arbitrary since procurement processes per se involve some flexibilities.

3.3.2 Specific procurement policies

Concerns have been raised that such procurement practices may constitute a "race-to-the-bottom", which may disincentivise suppliers who may leave the market [111–115]. In response, a more "strategic procurement" has been proposed, for instance, by WHO [18].

In parallel, the last two decades have seen a further **development of procurement tools**, supplemented in legislation, to react more appropriately to new challenges (see below chapter 3.3.2.3).

Purchase options that have been increasingly used as an option to grant access to new, usually high-priced medicines such as oncology medicines are managed-entry agreements (**MEA**). These MEA may complement discounts, rebates, claw-backs and paybacks that government mandates suppliers to grant to public payers. Further innovative purchase options are possible, including **delinking** the contracted health technologies from the volume. Vice versa, volumes may be **pooled**, and thus purchasing and negotiation power increases through the joint procurements of different providers, cross-regional, centralised and even cross-country (managed by national governments or international institutions.

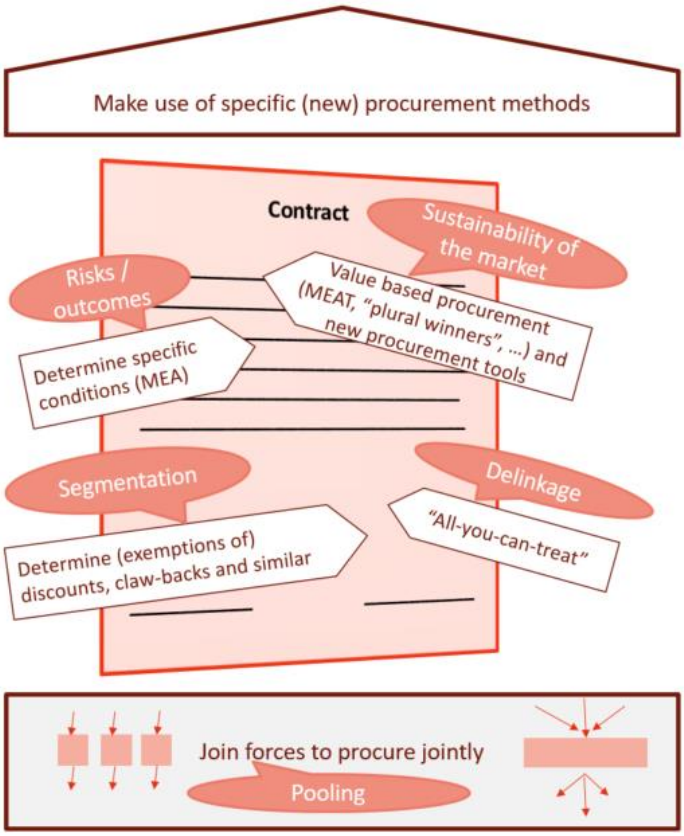
Table 3.12:
Results – Overview of standard and specific procurement policies for health technologies of the study countries, 2020

Procurement policies		Procurement features		Managed-entry agreements (MEA)		Exemption / reduction of discounts / clawbacks to public payers		Collaboration in procurement (joint procurement)		Value-based procurement (new procurement tools)		"All-you-can-treat" purchase contracts (delinkage)	
		medicines	*medical devices*	*medicines*	*medical devices*	*medicines*	*medical devices*	*medicines*	*medical devices*	*medicines*	*medical devices*	*medicines*	*medical devices*
Australia	outpatient	decentralised procurement by states and territories, pharmacy buying groups											
	inpatient	centralised elements at state or hospital level	centralised elements at state or hospital level										
Brazil	outpatient	centralised elements at national and regional level with obligation for open tenders in public sector											
	inpatient												
France	outpatient	national procurement agency and individual/joint procurement by hospitals											
	inpatient												
Germany	outpatient	tendering and contracting by social health insurance (mainly for generics)	procurement by social health insurance institutions via "open book" contracting										
	inpatient	procurement by hospitals											
Italy	outpatient	procurement by regional health authories and through central procurement agency											
	inpatient	procurement by hospitals, regional health authories and through central procurement agency											
Saudi Arabia	outpatient	mainly centralised procurement / tendering											
	inpatient												
South Africa	outpatient	centralised procurement for public facilities (public competitive tender and price negotiations)	procurement by public facilities										
	inpatient												
South Korea	outpatient	mainly individual procurement from manufacturer or wholesaler; tertiary hospitals mostly through competitive bidding process											
	inpatient												
Spain	outpatient	auction-like system for outpatient generics in few regions	procurement by regions and hospitals										
	inpatient	joint procurement at regional and national level through national procurement agency											
Turkey	outpatient	no tendering											
	inpatient	centralised procurement for public hospitals & individual procurement by hospitals											

Yes | Partly/Exceptionally | No and N/A (information not available)

Source: GÖ FP survey and literature

Figure 3.6:
Results – Taxonomy of specific procurement policies



Source and presentation: GÖ FP

Figure 3.6 provides an overview of specific procurement policies which can be overlapping (e.g. several countries list the enabling of MEA as a tool in procurement legislation). Below, the following specific procurement policies and purchase contract options will be presented:

» To set specific **conditions in the purchase contracts**, including linking payment for the health technology to the defined level of performance (e.g. health outcomes of the patients), thus performance-based **managed-entry agreements (MEA)**, which acknowledge the dearth of robust evidence (*risks/outcomes*),

» To determine **discounts, rebates, claw-backs and paybacks** that the seller has to grant to the purchaser (public payer), with reductions / exemptions for defined health technologies, patients, indications, etc. (*segmentation*),

» To conduct **value-based procurement** and to make use of specific **(new) procurement tools** allowed by national and supranational (e.g. EU) legislation, such as the "plural winners" system, MEAT, DPS, to ensure a *sustainable "healthy" market,*

» To conclude innovative purchase contract options (e.g. **Netflix model, "All-you-can-treat"**) based on the concept of *"delinkage"* from volume and

» To join forces (and volumes and procurement know-how) and to **procure jointly**, e.g. hospital purchasing groups, centralised procurement at federal level, cross-country procurement (*pooling*).

3.3.2.1 Managed-entry agreements

An increasing number of countries implemented MEA to allow the market entry of medicines, usually with high price tags (cf. Table 3.13). Brazil and South Africa are the two case study countries without a MEA. MEA for medical devices are less common but were concluded in Australia, France and Turkey. Typical indications of medicines under a MEA are oncology medicines and orphan diseases. Inclusion of antibiotics into a MEA was not reported from any study country. MEA are typically negotiated by the pricing authority to cover the whole country; in addition, hospitals (and hospital groups) conclude MEA at their levels.

As described in chapter 1.4, MEA are usually divided into financially-based MEA and performance-based MEA. Italy, which was one of the first countries introducing MEA, has a number of MEA. It also provides a third category of MEA, the so-called "appropriateness agreements" (cf. Box 3.12).

Box 3.12:
Results – A variety of managed-entry agreements in Italy

Italy – Managed-entry agreements

Starting in the first years of the new millennium, Italy was one of the first countries which concluded managed-entry agreements (MEA). It is probably the (European) country with the highest number of MEA, including performance-based MEA.

They are negotiated between the Italian Medicines Agency AIFA and the marketing authorisation holder. The regions and hospitals do not conclude MEA on their own.

There are MEA at patient level and MEA at population level.

The first group comprises Payments by Result and Risk Sharing (both performance-based MEA) as well as Cost Sharing and capping models (financially-based MEA). AIFA Monitoring Registries have been implemented for all these MEA at patient level. The rationale of monitoring registries is to ensure and manage prescribing appropriateness. In 2019, there were 194 monitoring registers at the web platform. MEA at population level, which include spending caps, are monitored by data on NHS expenditure and consumption.

For Italy, information on which medicines are subject to an MEA is published. Usually, the type of the MEA is also published. Discounts tend to be confidential and are only known to the public institutions involved (e.g. the regions as public payers) and the manufacturer.

Source: GÖ FP survey

Table 3.13:
Results – Examples of specific procurement policies: managed-entry agreements

Procurement policies		Managed-entry agreements (MEA)	
		Medicines	*Medical devices*
Australia	outpatient	**Yes** (special pricing arrangements incl. rebates / reimbursement caps, Coverage with Evidence)	**No**
	inpatient	**Yes** (individual or collaborative on hospital or state level)	
Brazil	outpatient	**No**	**No**
	inpatient		
France	outpatient	**Yes** (financially-based and performance based MEA concluded by Pricing Committee and in hospitals, conditional pricing for low-value medicines, but suspended in 2016)	**Yes, but few** (some price-volume agreements)
	inpatient		
Germany	outpatient	**Yes** (MEA mainly for generics, price-volume agreements between SHI and manufacturer)	**No**
	inpatient	**Yes** (MEA at hospital level)	**N/A**
Italy	outpatient	**Yes** (many MEA (financial MEA, performance-based, appropriateness agreements, with registries)	**No**
	inpatient		
Saudi Arabia	outpatient	**Yes** (centralised, to be extended)	**No**
	inpatient		
South Africa	outpatient	**No**	**No**
	inpatient		
South Korea	outpatient	**Yes** (different types of risk sharing arrangements)	**N/A**
	inpatient		
Spain	outpatient	**Yes** (several MEA)	**No**
	inpatient		
Turkey	outpatient	**Yes** (financially-based MEA for personalized and high-priced medicines – so-called "alternative reimbursement model")	**Yes** (MD and in vitro diagnostics (IVD) in the scope of the alternative reimbursement models)
	inpatient		

MD = medical devices, MEA = managed-entry agreement, N/A = information not available / no example identified

Source: GÖ FP survey

3.3.2.2 Exemptions and reductions from mandatory discounts and claw-backs

MEA may include different forms of pay-backs and claw-backs of supplier to the public payer. In addition, mandatory claw-back and discounts may be provided for in legislation.[18] This is the case in five of the study countries (France, Germany, Italy, South Korea, and Spain), where pharmaceutical manufacturers are required to grant mandatory discounts to the public payers. These discounts are usually published in legislation and their amount is known. For medical devices, a claw-back system only exist in France.

Some of the countries with mandatory discounts provide exemptions and reductions for defined medicines (cf. Table 3.14). Orphan medicines, innovative medicines and generics are a common case. Spain, for instance, asks a lower mandatory discount for orphan medicines than for other medicines. In Germany, generic medicines included in the reference price system (internal price referencing) are exempt fron the statutory discounts. France used to have an exemption from the statutory claw-back for orphan medicines and generics, but this was abolished in 2019. Italy also exempts orphan medicines from the payback manufacturers are required to pay in case of exceeding the national budget; in addition, medicines considered to be innovative (thus eligible for one of the two "innovation funds", cf. Box 3.8) are exempt from a mandatory discount on the medicine price. In South Korea, the mandatory discounts is only valid after three years in the case of locally produced medicines (cf. Box 3.13).

Box 3.13:
Results – Privilege to nationally produced medicines through postponed discounts in South Korea

Korea – Postponement of discounts for national production

As a rule, if the volume of a medicine provided under a price-volume agreement exceeds the volume anticipated in the agreement within one year after the medicine's inclusion in South Korean's reimbursement list, then price renegotiations will need to be held and the price of the medicine adjusted accordingly.

However, exemptions from this rule apply for locally developed new medicines with a perspective to entering the global market. These medicines are eligible for a price-volume-based refund system, which allows the price reduction according to the price-volume agreement to be postponed for three years. After three years, a defined amount will be refunded to the National Health Insurance Service (NHIS).

Source: GÖ FP based on a survey with competent authorities

[18] Paybacks and claw-backs are examples which highlight the overlapping features of reimbursement, pricing and procurement policies. These polices could also be classified as reimbursement policy, since it concerns public funding. It might also be considered as a pricing policy since it may impact the price. For the purpose of this study, it was classified as a procurement policy since it is a similar mechanism to the purchasing mechanism of an MEA.

Table 3.14:
Results – Examples of specific procurement policies: exemptions from and reductions of mandatory discounts and claw-backs to public payers

Procurement policies		Exemption / reduction of discounts / claw-backs to public payers	
		Medicines	*Medical devices*
Australia	outpatient	**No** (statutory price reductions, no exemption)	**No**
	inpatient	**No**	
Brazil	outpatient	**No**	**No**
	inpatient		
France	outpatient	**Exemptions abolished** (industry claw-back based on turnover (since 2019: no longer different rates for different sectors, exemptions for generics and orphan medicines abolished)	**No** (since 2020 claw-backs for MD, no exemption)
	inpatient		
Germany	outpatient	**Yes** (exemption from statutory discounts for medicines included in the reference price system, thus those with comparators)	**No**
	inpatient	**No**	
Italy	outpatient	**Yes** (statutory discounts to NHS, exemption for medicines considered innovative; orphan medicines except from payback (in case of exceeding national budgets))	**No**
	inpatient		
Saudi Arabia	outpatient	**No**	**No**
	inpatient		
South Africa	outpatient	**No**	**No**
	inpatient		
South Korea	outpatient	**Yes** (postponement of the discount under the price-volume agreement for a period of 3 years for locally produced medicines)	**N/A**
	inpatient		
Spain	outpatient	**Yes** (statutory claw-back by industry, wholesale and pharmacy (shared) to NHS, lower for OMP than for other new med., highest share for med. > 10 years in the market; exemption from price-volume agreements for medicines with little budgetary impact)	**No**
	inpatient		
Turkey	outpatient	**No** (mandatory discounts to social insurance – no exemption)	**No**
	inpatient		

MD = medical devices, N/A = information not available / no example identified, NHS = national health service, OMP = orphan medicinal products

Source: GÖ FP survey

3.3.2.3 Value-based procurement and new procurement tools

In recent years, new procurement tools have been introduced, which comprises a range of mechanisms (cf. Table 3.15).

Table 3.15:
Results – Examples of specific procurement policies: value-based procurement (new procurement tools)

Procurement policies		Value-based procurement (new procurement tools)	
		Medicines	*Medical devices*
Australia	outpatient	**Yes** (procurement of non-formulary medicines – high-cost medicines and those for reserved treatment, e.g. antibiotics, upon a defined approval process)	**No**
	inpatient		**No**
Brazil	outpatient	**Yes** (emergency purchases (in particular court-ordered purchases in face of death risk) and single source medicines waived from tendering)	**No**
	inpatient		
France	outpatient	**N/A**	
	inpatient		
Germany	outpatient	**Yes** (tendering for generics based on the tool of "open-house contracts" with all interested suppliers)	**Yes** ("open book" contracting)
	inpatient	**N/A**	
Italy	outpatient	**Yes** (use of DPS by centralised procurement agency)	
	inpatient		
Saudi Arabia	outpatient	**Yes** Full funding of the proposed price if a medicine fulfils the criteria set by the procurement agency	**No**
	inpatient		
South Africa	outpatient	**No**	**No**
	inpatient		
South Korea	outpatient	**No**	**N/A**
	inpatient		
Spain	outpatient	**Yes** (use of new methods in tendering (e.g. dividing contracts in lots)	
	inpatient		
Turkey	outpatient	**N/A**	
	inpatient		

DPS = dynamic purchasing system, N/A = information not available / no example identified

Source: GÖ FP survey

In EU Member States, for instance, EU legislation offered new tools, and this was translated into national legislation (see the example of Spain in Box 3.14). The EU procurement legislation introduced, for instance, the "Most Economically Advantageous Tender" (MEAT) concept, which allows considering other criteria beyond the price. Other examples are procurement tools such as framework agreements (two-stage procurement processes, with a kind of mini-competition in the second stage of individual call-offs) and the electronic variant of "dynamic purchasing system" (DPS), as introduced in Italy (cf. Table 3.15). Introduction of MEA (particularly concluded at national level between the public authority and the company) typically also requires a change in (procurement) legislation (as the Spanish example shows). Looking beyond the case study countries to further EU countries, such legal changes have been taken place over the last ten to five years (unpublished PPRI information).

Box 3.14:
Results – Introduction of new procurement tools in Spain

Spain – Procurement novelties

The 2017 reform of the Public Sector Procurement Law (Ley de Contratos del Sector Público / LCSP) allowed innovative elements to be included in procurement procedures, such as risk-sharing agreements, expenditure ceilings and results-based payments. The reform also allowed establishing a new relationship between the marketing authorisation holder and public health administration, thus introducing new, more collaborative elements that seek the sustainability of the system and patient interests.

Novelties include:

» *In the traditional procurement procedures:* in open procurement, novelties consist of the new principle of dividing the contract into lots, regulations governing the Most Economically Advantageous Tender (MEAT) and the presence of social, labour and environmental responsibility criteria; an extraordinary procurement with unannounced negotiation procedure (transparency on the implementation of the procedures)

» *In electronic procurement procedures*: Dynamic Procurement System (DPS) and electronic auction

» *Exploiting savings potentials* in Framework Agreements run by the national procurement agency INGESA by opening some lots in the second stage in concurrent bids

» *New procedures:* 1) negotiated tender procedure (procedure of successive stages of negotiation that allow the objective to be specified and the selection of the most advantageous economic tender), 2) simplified open procedure (within one month after publication), 3) preliminary market consultations and 4) innovation association (allowing bidders to establish an association of bidders to carry out research to develop specific solutions.

Source: GÖ FP survey and literature [116, 117]

While EU Member States have the possibility to use new tools provided for in EU and thus national procurement legislations, this is up to the countries to decide which of the new procurement options they actually use [118].[19]

Not only in Europe, but globally there is the discussion to move away from the prices as the sole award criterion and to consider other aspects. In South Africa, for instance, health technologies from national production are privileged in tender (cf. Box 3.15).

Box 3.15:
Results – Premium tender prices for national production in South Africa

South Africa – premium tender prices for national production

When awarding the winning tender contracts, the South African national government uses a scoring system. The government may consider other factors than the lowest price, which usually accounts for 90 of 100 points needed for awarding the contract. For example, the government may be willing to award a premium corresponding to up to 10 points to national medicine manufacturers to promote local economic growth, job creation and a positive trade balance, foreign multinational firms and their local subsidiaries are not eligible for this premium.

Source: GÖ FP survey

Overall, the concepts of "dual-winners" and "plural-winners" systems have been promoted in procurement. The rationale is that not only the sole winning bidder gets awarded but also a second and even further bidder, possibly with defined quota or at a lower price ("divide-the-pie" strategy). This ensures that in case of delivery failures of the winning bidder back-ups solutions are in place to ensure availability. It also lowers the risk losing bidder withdrawing from the market which is no longer considered attractive. These procurement tools that aim to ensure sustainability and "a healthy market" and consider value as an overarching concept (instead of simply the lowest price) are summarized under the concept of value-based procurement (or outcome based procurement) [119–122].

In Brazil, emergency purchases in the face of death risk and on-patent medicines are waived from tendering. For the emergency purchases it frequently occurs after court sentences, a phenomenon described as judicialization (cf. Box 3.16).

[19] The survey was performed for the case study countries, thus it is not known to which extent novel procurement tools have been implemented in further EU Member States. A recent evaluation of the centralised procurement for medicines in Portugal confirmed that the national leval provisions (e.g. MEAT criterion) allow their application but they are not fully exploited in practice.

Box 3.16:
Results – Judicialization in Brazil

Brazil – Judicialization of access to medicines

Patients filing lawsuits against the state to get access to and funding for medicines occurs frequently in Brazil and also further Latin American countries (compared to other countries globally). As a result, this phenomenon has been given a special name: "judicialization". It is a contested and hot debated topic.

The court cases are filed based on the right to health which is defined as an unlimited right in the constitution, and for any policy measure aiming to limit it constitutes a violation.

Lawsuits to be granted access to medicines at the expense of the public payer are a commonly judicialized service (following access to intensive care unit) in Brazil, and it frequently concerns high-priced medicines. Although it is argued that it mainly serves urban elites, there is some evidence that it has helped grant access for some low-income people.

They are case-by-case decisions, and evidence from Brazil shows that requested medicines were granted in the majority of cases. While this ensures access to medicines to individuals, it challenges the policy rationale when limiting or restricting conditions imposed for clinical and rational use reasons are overhauled. Requested medicines included some which had not been included in the Brazilian National Essential Medicines List and those with inconsistent evidence on efficacy [123]. Moreover, it has been argued that the court decisions "violate health rules" [124]. This eventually weakens implementation of policies.

Another major argument in the debate is that the judicialization increases the "health inequity" since scarce resources of the health budgets are diverted to funding of high-priced medicines claimed by – some say: already privileged – individuals instead of being invested into basic sanitation, primary health care or vaccination programmes which benefit broadly.

Source: GÖ FP survey and literature [123–130]

3.3.2.4 Delinkage models

One of the study countries, Australia, negotiated a contract for hepatitis C, in which the procured medicines is "delinked" from the volume (cf. Box 3.17). For no other study country a delinkage model was identified.

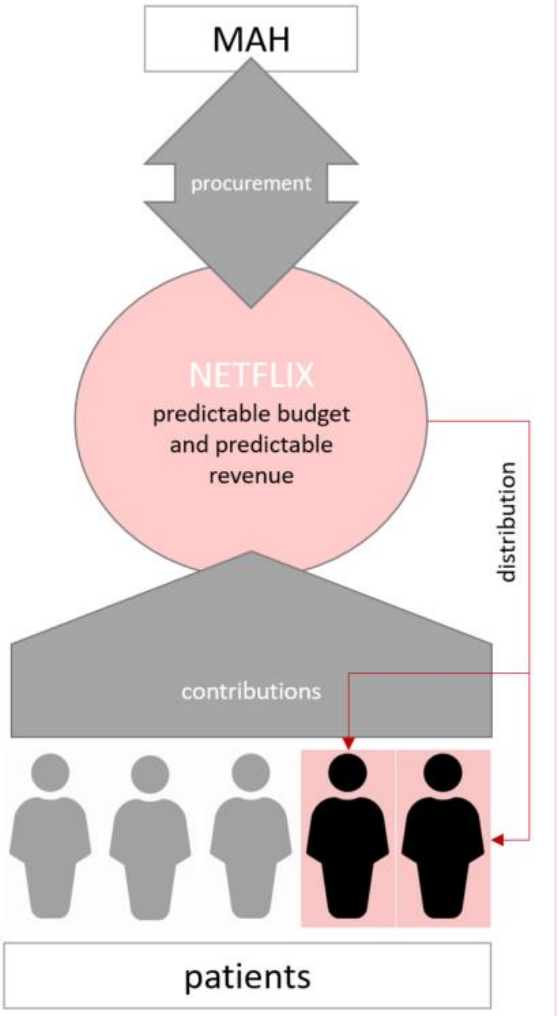
Box 3.17:
Results – "Netflix" model for Hepatitis C medications in Australia

Australia – Flat-rate contract for Hepatitis C medicines

The Australian government contracted a five-year agreement with five manufacturers for unlimited use of hepatitis C medicine.

Australia is aiming at eliminating hepatitis C as a public health threat by 2030. Therefore, the Australian government concluded a deal with pharmaceutical companies to treat an unlimited number of people with hepatitis C for 1 billion Australian dollar between March 2016 and 2020 (with low out-of-pocket payments to the patient).

The so-called Netflix model pools contributions to generate a predictable budget and predictable revenue for the market authorisation holders.



Source: GÖ FP survey

3.3.2.5 Pooling and collaboration in procurement

Joining forces of procuring entities can be done at different levels. Collaboration of hospitals (or hospital groups) is common in several of the study countries (e.g. Australia, France, Germany). In France, for instance, there are joint procurement initiatives of several hospitals, based on geography (collaboration in a region; e.g. "Réseau des acheteurs hospitaliers d'Ile de France" (RESAH-IDF), others related to specialised care centres e.g. Regional Cancer Centers (UNICANCER). In countries with regionalised health services (e.g. Italy, Spain) procurement is frequently done at the level of the regions. This is usually done for both medicines and medical devices (cf. Table 3.16).

Table 3.16:
Results – Examples of specific procurement policies: collaboration in procurement (joint procurement)

Procurement policies		Collaboration in procurement (joint procurement)	
		Medicines	*Medical devices*
Australia	outpatient	**Yes** (pharmacy buying /franchising groups)	
	inpatient	**Yes** (among hospitals)	
Brazil	outpatient	**Yes** (all levels)	
	inpatient		
France	outpatient	**Partly** (few examples of centralised procurement at national level, e.g. vaccines during the H1N1 epidemic	
	inpatient	**Yes** (among hospitals)	
Germany	outpatient	**Partly** (procurement collaboration of social health insurance institutions)	**Partly** (procurement collaboration of social health insurance institutions, only for medical aids)
	inpatient	**Yes** (among hospitals)	
Italy	outpatient	**Yes** (regional level, centralised procurement, member of Valletta Declaration (planned joint cross-country procurement))	
	inpatient		
Saudi Arabia	outpatient	**Yes** (centralised procurement on national level, member of the Gulf Cooperation Council which performs joint cross-country procurement for essential medicines and medical supplies)	
	inpatient		
South Africa	outpatient	**No**	**Exceptionally** (hospitals in hospital networks)
	inpatient		
South Korea	outpatient	**No**	**N/A**
	inpatient		
Spain	outpatient	**Yes** (regional level, centralised procurement, member of Valletta Declaration (planned joint cross-country procurement)	**Yes** (same as for medicines, apart from Valletta Declaration)
	inpatient		
Turkey	outpatient	**No**	**No**
	inpatient		

N/A = information not available / no example identified

Source: GÖ FP survey

In some of the study countries, the national procurement agency is also in charge of procuring medicines and medical devices. The scope differs among the countries: While Saudi Arabia procures a large number of medicines via the national procurement agency, the Spanish procurement agency uses framework agreements for the following four groups: epoetin, recombinant factor

VIII, immunosuppressants and antiretrovirals. The Spanish regions are allowed to join in the centralised procurement. The Italian national procurement agency uses the procurement tool of "dynamic purchasing system" (DPS), a kind of electronic "framework agreements" for medicines with competitors (e.g. generic market).

Furthermore, governments can also collaborate cross-country. For instance, Italy and Spain joined the cross-country collaboration "Valletta Declaration", which aims to jointly procure high-priced medicines (no joint procurement has yet been done). Cross-country procurement can also be facilitated by an international institution, such as WHO or UNICEF. Examples include the PAHO Strategic Fund and Revolving Fund, to which Brazil is a member, and the Gulf Cooperation Council (GCC) joint purchasing programme, in which Saudi Arabia participates (cf. Box 3.18).

Box 3.18:
Results – Regional pooled procurements in the Americas and Persian Gulf

Brazil – Strategic Fund and Revolving Fund of the Pan American Health Organization

The Pan American Health Organization (PAHO) offers pooled procurement for medicines and supplies included in the World Health Organization (WHO) Model List of Essential Medicines through its Strategic Fund and for vaccines, syringes and related supplies through the PAHO Revolving Fund.

As of June 2020, 34 countries and territories in Latin America and the Caribbean have signed agreements with PAHO to use the mechanism of the PAHO Strategic Fund.

The PAHO Revolving Fund dates back to 1979. The mechanism involves a common, revolving fund that allows PAHO to pay producers before countries reimburse the Fund (sometimes in local currency). With the working capital always present in the Revolving Fund, PAHO purchases supplies in advance of payment, as long as the country pays the Fund back within 60 days. At no cost to the country, PAHO negotiates prices, draws up contracts with suppliers, arranges shipping, and handles other administrative procedures to ensure safe arrival to the country.

Saudi Arabia – Gulf Cooperation Council joint purchasing programme

The Gulf Cooperation Council (GCC) is an interregional collaboration of the Persian Gulf States Bahrain, Kuwait, Oman, Qatar, Saudi Arabia and the United Arab Emirates. It was officially established in 1982 as a regional economic and policy cooperation group dealing with trade, health, agriculture and education, following on a previous collaboration (called the Health Ministers Council). Among others, the countries collaborate in pharmaceutical regulation and policy. They have a harmonised marketing authorisation procedure and they collaborate in pricing.

Already in 1978, a first joint tender was launched to purchase 32 medicines. Over the years, several joint tenders were launched (e.g. ten tenders involving approximately 8,900 products between 1978 and 2003).

The procedures are done on an annual basis, with collecting and reviewing the countries' needs estimate during the Tender Preparation Committee meeting (usually held every March). The GCC Secretariat is in charge of preparing the documents and invited bidders. Only manufacturers pre-qualified by the GCC are invited to submit bids. All bidder candidates have to nominate a

local agent in Saudi Arabia, who will respond to the tender and act on behalf of the company. After a bidding period of 30–45 days, a Tender Opening Committee meets to open all sealed bids publicly and record the offers.

Assessment of progress made

PAHO Funds and the GCC group purchasing programme have grown importantly.

Reported achievements include savings since lower prices could be obtained due the pooled volumes. Furthermore, pooled procurements helped to achieve continuous supply.

Important prerequisites for success include a flexibility in country participation, quality assurance and control (partially even considered to be more important than the price), attractive payment terms, credibility and transparency in the procurement process and countries' participation in decision-making [131, 132].

Source: GÖ FP survey and literature [131–140]

The EU Member States France, Italy and Spain joined the Joint Procurement Agreement (JPA) of the EU which is a mechanism to jointly procure medical countermeasures (cf. Box 3.19).

Box 3.19:
Results – Joint Procurement Agreement of the EU

EU procurement for medical countermeasures

The Joint Procurement Agreement (JPA) for medical countermeasures was developed in response to the H1N1 pandemic influenza which highlighted weaknesses in the purchasing power of EU Member States.

In 2014, the European Commission approved the JPA, and soon several EU Member States joined. As of April 2020, the JPA has been signed by 37 countries, including all EU Member States.

A joint procurement procedure can be initiated if at least four EU Member States and the European Commission are willing to participate.

The JPA aims to improve the preparedness of the Member States to serious cross-border threats to health. Thus, scope of the JPA is medical countermeasures, such as vaccines and antivirals. The European Commission considered the signature of the framework contracts for pandemic influenza vaccines in March 2019 as a major achievement under the JPA.

In the beginning, there was discussion as to whether the JPA instrument could also be used to jointly procure high-priced medicines (such as orphan medicines, oncology medicines). However, it was made clear that this was not possible since the JPA aimed at procuring medical countermeasures.

COVID-19 vaccines

Little information is available regarding the joint procurement of COVID-19 vaccines in the EU.

The European Commission has concluded agreements with four pharmaceutical companies which allow purchasing COVID-19 vaccines once they receive marketing authorisation.

Source: [141–144]

4 Discussion

The study has aimed to identify policy options from the areas of reimbursement, pricing and procurement that can be used to incentivise market entry and uptake of new AMR health technologies. These include policies in place, abolished and being introduced for antibiotics and (rapid) diagnostic tests as well as for other health technologies with similar features. In the following, the authors will present the policy options identified in their survey (for the case study countries) and in the literature (examples from further countries, cf. chapter 4.1), assess them, also with regard to possible transferability to AMR health technologies (cf. chapter 4.2), and discuss pathways for the future (cf. chapter 4.3).

4.1 Overview of identified policy options

Upon marketing authorisation (of a medicine) or certification (of a medical device), a public authority usually has to take important reimbursement, pricing and/or procurement decisions. This is to ensure in-time, equitable and sustainable access to a health technology that is affordable to the patient and the health system and that, at the same time, provides sufficient return for the supplier to incentivise launch, production and supply.

4.1.1 Importance of the policy design

Broadly speaking, the **decision-making process of public authorities in the peri-launch phase** (between marketing authorisation / certification and launch) is as follows: As a prerequisite for inclusion into the **reimbursement** system (i.e. public funding), a health technology has to **demonstrate superiority** to existing alternatives in the system.[20] This is usually expressed in terms of the **"added therapeutic benefit"** (i.e. based on clinical outcome parameters) of the health technology compared to competitors. For health technologies that are identical or comparable to those already included in reimbursement (e.g. generic and biosimilar medicines), it is frequently sufficient to demonstrate a so-called "**economic advantage**" (e.g. a defined percentage rate of price reduction) to those in the reimbursement list. In addition to reimbursement for single health technologies (**individual reimbursement**), it is also possible to have **bundled reimbursement** through tariffs to remunerate the performance of services. One example of this is the diagnosis-related groups (**DRG**) system in hospitals. To ensure that the public payer and/or the patient pays an acceptable price for the health technology, **price regulation** is used. It aims to set affordable prices by applying different criteria (e.g. consideration of prices of other health technologies, prices in other countries, therapeutic benefit, production costs) to justify the pricing decision. The decision on the

[20] This is a major distinction to the marketing authorisation for which a medicine must "solely" prove its safety, quality and effectiveness – in comparison to placebo (cf. also chapter 1.4). Requirements for certification of medical devices tend to be lower and can differ depending on the purpose and risk class (e.g. in the EU).

reimbursement status and reimbursement price of a health technology can be substituted by a **procurement** process in which public procurers (at federal, regional or facility levels) decide whether and at which price, a health technology will be purchased for use in public health care.

This simplified description of the "general" or "standard" pharmaceutical system at the peri-launch stage shows the existence of **"flexibilities" in the policies**, as different criteria for reimbursement, pricing and procurement decisions (e.g. price, clinical parameters, societal and ethical considerations) can be applied. As such, the possibility of **incentives** to market entry and rewards for investments and innovation has already been built in to some policies, and they can be triggered by political decisions.

As explained (cf. chapter 1.4), there is frequently **not one policy** with distinct features, but **most reimbursement, pricing and procurement policies can be flexible**. Different designs will have different impacts. This allows adapting the policy options in order to comply best with the intended policy objectives. These objectives may vary between countries (e.g. stronger focus on supporting (local) industry versus cost-containment or encouraging competition, prioritisation for specific (vulnerable) patient groups and diseases) [69]. In any case, the overall objective of reimbursement, pricing and procurement policies is not solely cost-containment. Ensuring the financial sustainability of a publicly funded health system is one policy goal for which public payers are the responsible actors, but it is part of the overall aim to improve patient access to essential medicines [145].

Given the "flexibility in design" of reimbursement, pricing and procurement policies for health technologies, innovative models to be identified for the purpose of this study are not necessarily new policies. In some cases, they are adaptions or modifications of existing policies or methodologies or exemptions.

The analysis of the reimbursement, pricing and procurement policies in the study countries identified a total of 16 specific policy options (six in reimbursement, five in pricing and five in procurement) that could be used to incentivise market entry of health technologies. In Figure 4.1, the specific policy options were categorised into the strands:

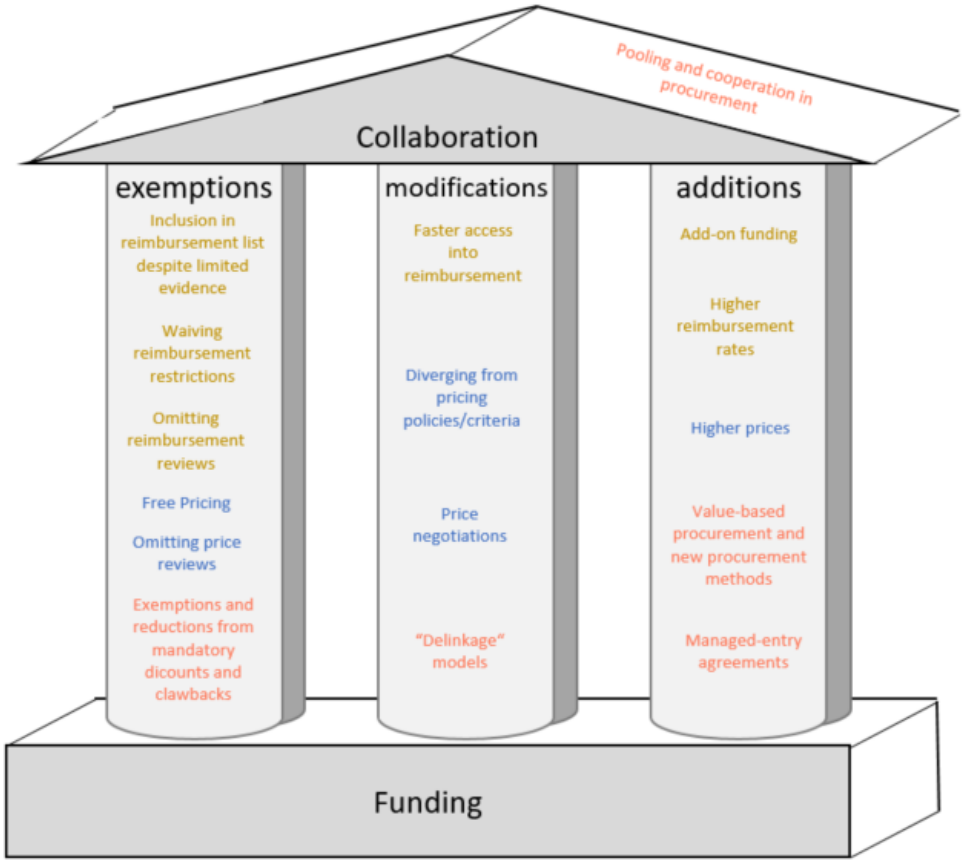
» **Exemptions** (e.g. higher prices / premium prices, higher reimbursement rates, exemptions from mandatory discounts and claw-backs to public payers, exemptions from proof of evidence)

» **Modifications in methods and processes** (e.g. related to value assessments such as HTA, procurement tools including new methods such as the "Most Economically Advantageous Tender" as award criterion and the "Dynamic Purchasing System", new purchasing contracts based on delinkage models and (outcome-based) managed-entry agreements

» **Additions** (e.g. additional funding sources such as specific budgets (funds) for defined medicines or funding for hospital medicines on top of DRG, so-called "DRG carve-outs")

In practice, the extent of implementation varied among the policy measures (cf. chapter 4.1.3, in particular Table 4.1) and also countries.

Figure 4.1:
Discussion – Tool box of possible specific policy options to incentivise market entry of AMR and similar health technologies



Colours indicate the policy area: yellow – reimbursement, blue – pricing, red – procurement

Source: GÖ FP based on the survey in the study countries

4.1.2 Overlaps across reimbursement, pricing and procurement policies and beyond

The colours used for the specific policy options in Figure 4.1 indicate the policy area to which they were classified in this study. Other studies [61–67, 69, 70, 84, 102, 146–150] use the same or similar taxonomies but also different classifications of some other terms. Different approaches can be applied and are justified.

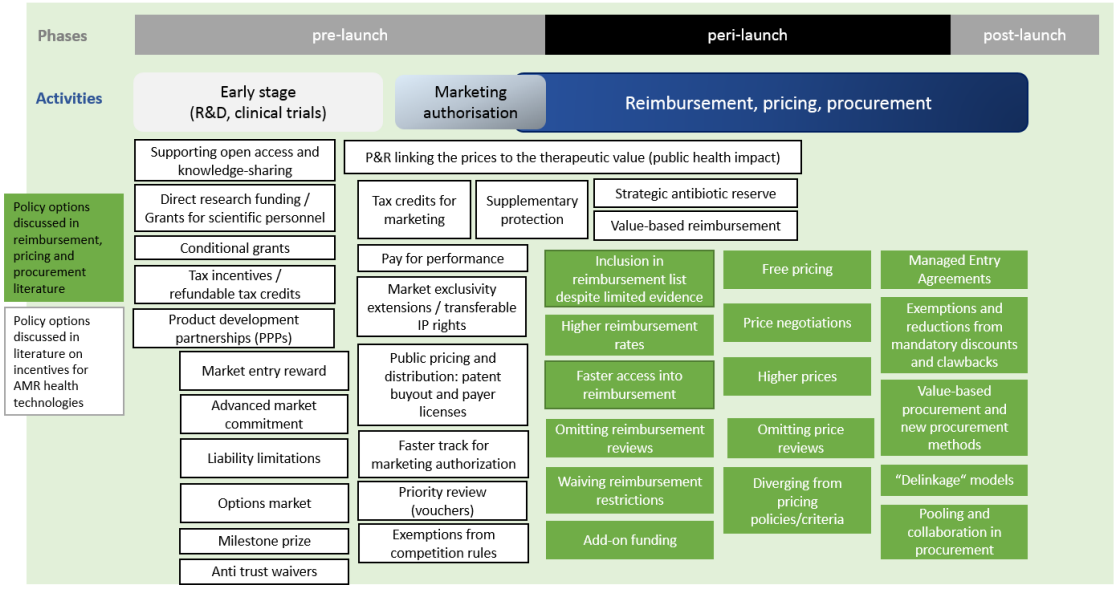
In addition, there are also overlaps between reimbursement, pricing and procurement policies and incentives for R&D (see Figure 4.2: proposals for incentivising R&D and market entry of AMR health technologies as identified in the literature and in this study). The AMR R&D incentive literature

mentioned terms such as “premium pricing” [151] and value-based reimbursement [152], which is rather terminology of the “reimbursement, pricing and procurement policy world”. In this study, these overlaps will be dealt with as follows:

» **“Premium pricing”:** In AMR literature and debate, this concept is usually sugested to be implemented through the outcome-based pull mechanism of a **market entry reward (MER)**, which can be implemented through a “(premium) pricing model” or an “insurance model”, with or without a delinkage component. MER are not scope of this study (which focused on existing national policies), but the concept of “premium prices” (i.e. higher prices, even despite limited evidence and data) will be addressed below in chapter 4.2.3.

» **Value-based reimbursement:** In this context, this relates to setting the reimbursement price (i.e. the amount covered by a public payer) based on the **assessment** of its value to society (societal value). In chapter 4.2, value assessment frameworks (e.g. HTA) will be addressed but the term “value based reimbursement” will not be used due to ambiguity of the definition.

Figure 4.2:
Discussion – Overview of policy options to incentivise R&D and market entry of AMR health technologies identified in the literature and in this study



Source: [4, 30–34, 38, 41, 43, 44, 64, 65, 69, 74, 85, 151–153] and GÖ FP based on the survey, presentation: GÖ FP

4.1.3 Specific reimbursement, pricing and procurement policy options globally

The survey performed for this study aimed at identifying reimbursement, pricing and procurement policy options that could incentivise market entry and production of AMR health technologies and

of health technologies with similar features in ten selected case study countries. As described in the methods chapter (cf. chapter 2.2), this was done based on pre-filled fact sheets on the country policy frameworks, with specific questions to "dig deeper". It is acknowledged that some existing interesting examples might not have been identified.[21]

A more important limitation, however, is that due to the methodological decision to select case study countries, **further interesting examples in other countries** were not covered in the primary data collection. To account for this possible shortcoming, the authors looked for further examples of specific policy options.

Table 4.1 lists specific policy options identified in both case study countries and beyond. The examples in Table 4.1 are not exhaustive; they are intended to be illustrative and provide ideas for policy-makers.

Table 4.1:
Discussion – Specific reimbursement, pricing and procurement policies to incentivise market entry of AMR and similar health technologies in the study countries and globally

Policy	Examples		
	Countries	Description	Sources
Reimbursement			
Inclusion in public funding without proof of evidence	**Germany**	Antibiotics are exempt from HTA and are thus automatically included in reimbursement	Box 3.3
	Australia, South Korea, Turkey	Waiving value assessments (HTA, pharmacoeconomic assessments) for orphan medicines	Ch. 3.1.2.1
	Germany	Innovative medical devices are exempt from "early benefit assessment"	Ch. 3.1.2.1
	Scotland	Lower levels of evidence (e.g. on efficacy and safety) and in economic evaluations for orphan medicines	[154]
Higher reimbursement (rates)	**France**	Higher reimbursement rates for outpatient medicines with higher therapeutic benefit and exemption from co-payments for outpatient medicines and medical devices for patients with defined severe and chronic diseases	Box 3.4
	Several European countries (e.g. Finland, Hungary, Poland, Portugal)	Higher reimbursement rates for outpatient medicines in case of higher therapeutic benefit and for defined patient groups (including exemption from co-payments)	[64]

[21] It could be argued that by sharing a pre-filled fact sheet instead of an empty questionnaire, no new information would be retrieved and included information only confirmed. To minimise this risk, the authors asked very specific questions (including on contradictory and misleading information found in the literature). Some of these requests for details could not be answered by the respondents. In the interviews the authors also asked open questions on possible incentivising policies and reported examples from other countries to bring to mind existing similar policies.

Policy	Examples		
	Countries	Description	Sources
Faster access into reimbursement	**Germany**	Immediate access to the market upon marketing authorisation, and reimbursement of a price set at the discretion of the MAH in the first year for all medicines, including antibiotics	Ch. 3.1.2.1
	7 study countries (e.g. Italy, South Korea)	Early access schemes (with different models of coverage) or faster access in reimbursement for medicines (7 study countries) and medical devices (3 study countries)	Ch. 3.1.2.3
	Slovakia, UK, some European countries	Models of early access schemes	[155], PPRI
Omitting reimbursement reviews	–	*No examples identified*	–
Waiving reimbursement restrictions / conditions of use	**Australia**	Revised strategy on repeated prescribing of certain antibiotics	**Box 3.6**
	Germany	Laboratory diagnostics for antibiotics are exempt from "profitability control", thus unlimited use without justification is possible	Ch. 3.1.2.5
Add-on funding	**Italy**	2 innovation funds for innovative oncology and non-oncology medicines	Box 3.8
	England	Cancer Drug Fund	Box 4.3
	France, Germany, Austria, further countries	"DRG carve-out": additional funding for hospital medicines on top of the DRG system	Box 3.7, PPRI
		Pricing	
Free pricing	**Germany**	For all medicines in the first year after launch (but indirect price control for procured medicines in hospitals)	Box 3.9
	7 study countries and several further countries (e.g. Croatia, Czech Republic, Estonia, Finland, **France**, Hungary, Ireland, **Italy**, Latvia, Poland, Russian Federation, Slovakia, Slovenia, **Spain**, Sweden, Switzerland, **South Korea**)	Free pricing for non-reimbursable medicines	Ch. 4.2.3.2, [65], PPRI
	UK	For all medicines (but indirect price control through profit control)	[65]
	France, South Korea and Spain	For non-reimbursable medical devices	Ch. 3.2.2.1
	Remaining study countries	For all medical devices (but indirect price control for procured medical devices)	Ch.3.2.2.1
Price negotiations	**10 study countries** and many further countries	In all study countries for medicines and in 6 study countries for medical devices Whenever MEA are concluded	Ch. 3.2.2.2, PPRI
Higher prices for defined HT	**South Africa**	For nationally produced medicines	Ch. 3.2.2.3
	South Korea	For biologicals	Box 3.10

Policy	Examples		
	Countries	Description	Sources
Omitting price reviews / price increases	*Country not to be mentioned*	Omitting annual price reviews in return for a lump sum payment by industry	PPRI
	Australia	Annual price increases for clinically important medicines granted	Ch. 3.2.2.5
Diverging from pricing policies / criteria	**Study countries** and beyond	By considering a value-based approach flexibility is possible	Ch. 3.2.2.4
Procurement			
Managed-entry agreements (MEA)	**8 out of 10 study countries (all but Brazil and South Africa)**	Existence of MEA (both performance-based MEA, (e.g. pay-for-performance, risk-sharing) and more frequently financially-based MEA (e.g. flat discounts, capping, etc.)	Ch. 3.3.2.1
	Many high-income countries	Both performance and financially-based MEA but the latter are more frequently used	[68, 85, 156, 157]
Exemptions / reductions from mandatory discounts	**4 out of 6 study countries** with industry claw-back to the public payers (2020)	Germany: exemption for medicines with comparators in the internal reference price system Exemption (Italy) and reduction for orphan medicines (Spain) South Korea: oostponement of discount for locally-produced medicines France: exemption for orphan medicines and generics existed, abolished in 2019	Ch. 3.3.2.2
Value-based procurement (new tools)	**At least 4 out of 6 study countries**	Application of new procurement tools (e.g. Italy, Spain)	Ch. 3.3.2.3
	All EU Member States	EU legislation allows application of new procurement tools such as dynamic procurement system (DPS), the principle of "Most Economically Advantageous Tender" (MEAT), actual status of implementation not known / not examined in this study	[118]
Delinkage model	**Australia**	5-years contract (2016-2020) with five manufacturers of hepatitis C medication	Ch. 3.3.2.4
	Sweden	Procurement pilot for antibiotics with delinkage element	Box 4.4
	England	Pilot of the "commercial model" - a procurement based on delinkage	Box 4.4
Pooled procurement	**Brazil** and further Latin American countries	PAHO Revolving Fund and PAHO Strategic Fund for pooled procurement for Latin American countries	Box 3.18
	Saudi Arabia and the other GCC countries (Bahrain, Kuwait, Oman, Qatar, United Arab Emirates)	Pooled procurement for essential medicines and medical devices	Box 3.18
	European countries, incl. study countries (e.g. Cyprus, Denmark, Estonia, **Italy**, Portugal, Norway, **Spain**)	Centralised procurement for (defined) medicines, frequently those used in hospitals and usually also for medical devices at national levels	[18, 118]
	Denmark, Norway, Iceland, Sweden	Cross-country procurement for "older" hospital medicines by the Nordic Pharmaceutical Forum	Box 4.5

Policy	Examples		
	Countries	Description	Sources
	Estonia, Latvia, Lithuania	Cross-country procurement of vaccines in the Baltic Procurement Initiative	Box 4.5
	EU Member States, including **study countries in the EU**	EU Joint Procurement Agreement of medical countermeasures and joint procurement of COVID-19 vaccines	Box 3.18

Ch. = chapter, GCC = Gulf Cooperation Council, HT = health technologies
Study countries are listed in bold

Source: GÖ FP survey (see sources in the Annex) and further literature [18, 49, 64, 65, 68, 85, 88, 118, 154-159] and unpublished information from the PPRI network

For AMR health technologies, only a few exemptions and incentives could be identified, in particular in Germany, France as well as in UK and Sweden. The research revealed that despite the scarcity of policy options specifically targeting AMR health technologies, specific policy options were identified in particular for orphan medicines, (high-priced) oncology medicines and also for generics.

4.2 Assessment of identified specific policy options

This chapter explores to which extent the identified policy options are able to address challenges that are specific to AMR health technologies. Based on this assessment, selected policies are discussed in the light of the literature.

4.2.1 Addressing challenges of AMR health technologies

Health technologies (medicines and medical devices) are not "normal commodity goods", as explained in chapter 1.3.1, but have specific features, in particular if used in a solidarity-based health system (positive and negative externalities, no price elasticity, information asymmetry, three-party system). In addition, market entry and uptake of AMR health technologies are linked to specific challenges (cf. chapter 1.3.3). Some of these challenges are also relevant for other groups of health technologies (e.g. orphan medicines). Table 4.2 provides an assessment at which of the identified specific policy options may address these challenges.

Specific reimbursement policy options mainly address the **challenge that some health technologies fail to provide data and demonstrate value**. As reiterated in this study, the purpose of "standard" reimbursement policies is to decide if available data (in particular added therapeutic benefit, or "economic advantage" to alternatives) justify the inclusion of the health technology into public funding. It has been argued [41, 49] that existing value frameworks do not sufficiently capture the specificities of AMR health technologies which offer in particular societal value. Below, the authors will discuss whether this is true and which adaptations in the HTA methodology would be needed. AMR health technologies struggle with the **dearth of data** which are required for a "standard" reimbursement process. Mechanisms such as add-on funding through dedicated budgets for defined health technologies, not linked to an assessment, are also used to address this challenge.

Table 4.2:
Discussion – Potential of specifc reimbursement, pricing and procurement policy options to address challenges specific to AMR health technologies

Ability of specific policy options to address certain challenges	Difficulty of the health technologies							
	To prove value		To generate sufficient revenue			To ensure "planning certainty"	To deal with fragmentation	
	Lack of data	Mismatch value assessment fr.	Overall low prices	Lower prices vs. competitor	Low volumes		Sectors (out-/ inpatient)	Levels (federal/ region/facility)
Reimbursement								
Inclusion in public funding without proof of evidence	√	(√)	√		√	√	(√)	(√)
Higher reimbursement (rates) despite limited evidence	√	(√)	√	√	(√)	√	(√)	(√)
Faster access in reimbursement	√	√			√	√	√	√
Omitting reimbursement reviews	√	(√)				√		
Waiving reimbursement restrictions	√				√	√		
Add-on funding	√	√	√	√	√	√	√	√
Pricing								
Free pricing	(√)	(√)	(√)[1]	√[1]	(√)		√	√
Price negotiations	√		(√)	√	(√)	√		
Higher prices for defined health technologies	(√)		√	√[2]	(√)	√	√	√
Omitting price reviews			√	(√)				
Diverging from pricing policies / criteria			√	√[2]	(√)			

Ability of specific policy options to address certain challenges	Difficulty of the health technologies							
	To prove value		To generate sufficient revenue			To ensure "planning certainty"	To deal with fragmentation	
	Lack of data	Mismatch value assessment fr.	Overall low prices	Lower prices vs. competitor	Low volumes		Sectors (out-/ inpatient)	Levels (federal/ region/facility)
Procurement								
Managed-entry agreements	√		(√)	(√)	(√)	**√**	√	√
Exemptions / reductions from mandatory discounts			√	√	(√)			
Value-based procurement / new procurement methods			√	√	√	**√**	√	√
Delinkage model			√		**√**	√		
Pooled procurement					**√**	√	√	√

fr. = framework

[1] However, free pricing is only able to meet this challenge if there is the ability-to-pay on behalf of the purchasers (patients for non-funded health technologies and public payers in case of reimbursed health technologies). Thus, if prices are too high to be affordable for patients, linkage to a reimbursement system is highly beneficial.

[2] The potential of this specific policy option depends on whether, or not, competitor health technologies are among those that are also granted higher prices or are allowed exemptions / modifications from pricing policies / criteria. In the latter case, the incentivising potential of the policy option is considerably lower.

Note: The table shows the perceived ability for specific policy options to address defined challenges that AMR (and some further) health technologies have. The ability was considered strong (tick in bold), given (tick) or limited / under specific conditions (tick in bracket). If a field is left empty, then either the policy is perceived to not be able address this challenge or the answer is mixed depending on the situation.

The challenge of lack of RWD/RWE, mentioned in chapter 1.3.3, was not assessed in this table since it is relevant to all new health technologies. It requires systematic data collection, which may be built in some policies such as MEA.

The assessment in this table should not be interpreted as recommendation for specific policy options since further aspects (e.g. possible risks, implementation requirements, …) must also be considered (discussed in the chapters below).

Source and presentation: GÖ FP

Specific pricing policies can help to address the **challenge** for AMR health technologies **to generate sufficient revenue**, impacting in particular the price component. However, their revenue potential depends to a major extent on the ability-to-pay and willingness-to-pay of the purchasers. Being allowed to charge high prices does not generate any revenue as long as no sales are made. Thus, "payment security" is important for the suppliers. This can be reached by including health technologies into reimbursement (since public payers can afford to pay higher prices than patients) and through specific procurement contracts with purchasers in case the initial prices are unaffordable even for public payers.

Thus, **specific procurement policy options** are appropriate to **ensure "planning certainty"** which is important for private actors. Depending on the specificities of the health technology (e.g. low volume products) and of the health system organisation (e.g. split of responsibilities and payers between settings), specific procurement policies also may have the potential to **address the challenges of low volumes** (e.g. offering recompensation) and **of low prices** (e.g. specific payment and funding models to ensure revenue).

4.2.2 Selected reimbursement policy options

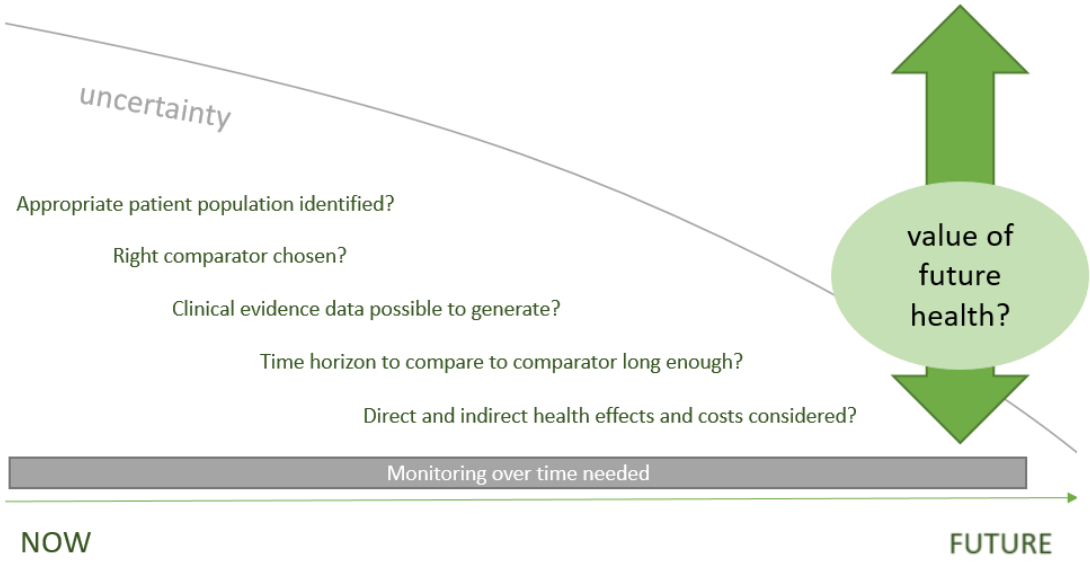
Following up on the pattern identified in Table 4.2 that AMR health technologies are confronted with an absence of evidence, which limits their proof of their value, the discussion will focus on the two policy approaches of possible changes with regard to the value assessments and on add-on funding. The chapter ends with a consideration of early access schemes.

4.2.2.1 Exemptions from and adaptions of health technology assessments

The specificities of AMR health technologies challenge health technology assessments (cf. Figure 4.3 for the value assessment of an HTA for novel antibiotics). In response, policy-makers may decide to exempt AMR health technologies from the HTA, or to adapt its methodology.

Some of the study countries opted to **lower the assessment requirements for the reimbursement decision** by **exempting defined health technologies from the value assessment** (in the following called health technology assessment / HTA), or at least from parts of it (e.g. exemption of the cost-effectiveness analysis, cf. chapter 3.1.2.1). For defined antibiotics, this exemption is applied in Germany; in other countries other health technologies which are likely to not meet requirements of the HTA process due to their specificities (e.g. orphan medicines) or which are given preference for other rationales (e.g. local R&D in South Korea) are exempt.

Figure 4.3:
Discussion – Challenges of performing an HTA for novel antibiotics



Source: [49], presentation: GÖ FP

For years, the challenges of performing an HTA for orphan medicines have been discussed, and some have argued against HTA for these medicines. In fact, so-called "ultra-orphans" (i.e. medicines to treat a disease affecting fewer than 1 in 50,000 [160]) are often not assessed by national HTA bodies [154].

Choosing the possibility of **exempting health technologies from value assessments will likely perpetuate the dearth of evidence**. An HTA allows collecting and considering (limited) data. Furthermore, if specific health technologies are known to be exempt from HTA, there is no incentive for companies to even try to generate any data.

Thus, the other response to the criticism that **common HTA methodologies do not sufficiently capture the specificities of AMR and similar health technologies** is to adapt the value assessment method. It must be remembered that HTA is a tool to support decisions on reimbursement and pricing which includes several components. As a tool, it is powerful, since the assessment can be designed in a comprehensive and targeted manner.

As explained in chapter 1.4, a full HTA as defined by the so-called "core model" of EUnetHTA (a collaboration on HTA in the EU, cf. Box 4.1) include analyses of the cost and economic effectiveness, ethical aspects, organisational aspects, patient and social aspects, and legal aspects [78]. This also allows for a comprehensive assessment.

Box 4.1:
Discussion – EUnetHTA collaboration and legislative proposal for future HTA collaboration

EUnetHTA: European Network for Health Technology Assessment

HTA agencies in European countries have been collaborating in the European Network for Health Technology Assessment (EUnetHTA) since its inception in 2007. EunetHTA was established in reaction of the European Commission and the Council of Ministers targeting HTA as a political priority and recognising the need for establishing a sustainable European network on HTA.

The aims of EUnetHTA include the support of collaboration between HTA bodies in European countries through the facilitation of efficient HTA resource use, the creation of a sustainable system of HTA knowledge sharing and the promotion of good practice in HTA methods and processes. A main accomplishment of EUnetHTA has been the development of a common methodology for evaluation the clinical aspects of new health technologies. The so-called "core model" for HTA provides practical guidance for performing HTA.

Over the years, the network has grown to 81 partner organisations of 29 countries. Co-funded by the European Commission, EUnetHTA has been organised in the form of joint actions (i.e. a cooperation between governments and researchers in EU Member States). The current Joint Action 3 was planned to end in 2020.

Legislative proposal of the European Commission on strengthening EU cooperation beyond 2020

With EUnetHTA JA 3 coming to an end, the European Commission tabled a proposal for future collaboration in HTA beyond 2020. On 31 January 2018 the European Commission published a draft regulation envisioning the centralised evaluation of clinical benefit for all new medicines and certain high-risk medical devices, while Member States would be obliged to refrain from performing duplicative country assessments.

The aimed adoption of the Regulation by 2019 could not be held. While the European Parliament adopted its position at first reading in February 2019 with an updated text, elections to the European Parliament in 2019 and COVID-19 pandemic starting in 2020 slowed down progress in the Council of the EU. It is now on the agenda of Portuguese Presidency of the Council of the EU (first half of 2021).

Source: [161-164]

Box 4.2:
Discussion – Transparent Value Framework to assess orphan medicines

Mechanism of coordinated access to orphan medicinal products: MoCA pilots to test a value framework

The Transparent Value Framework (TVF) was created to structure the discussion about the value of new orphan medicines, prior to national pricing and reimbursement submissions.

The TVF includes four criteria:

- unmet need,
- relative effectiveness,
- response rate and
- degree of certainty.

For each of the four criteria, a product can be scored using a categorical scale with three levels ("low", "medium", and "high").

Criterion	Lower Degree	Medium Degree	High Degree
Available Alternatives/ Unmet Need, including non-pharmaceutical treatment options	yes, new medicine does not address unmet need	yes, but major unmet need still remains	no alternatives except best supportive care - new drug addresses major unmet need
(Relative) Effectiveness, Degree of Net Benefit (Clinical Improvement, QoL, etc. vs. side effects, societal impact, etc.) relative to alternatives, including no treatment.	incremental	major	curative
Response Rate (based on best available clinically relevant criteria)	<30%	30-60%	>60%
Degree of Certainty (Documentation)	promising but not well-documented	plausible	unequivocal

The TVF was developed as part of the Mechanism of Coordinated Access to orphan medicinal products (MoCA) project, initially in the platform on access to medicines in Europe under Corporate Responsibility in the field of Pharmaceuticals. EU Member States, industry, patients' representatives and other stakeholders developed a potential mechanism for such cooperation. EU Member States adopted this concept as part of the formal conclusions of the Process on Corporate Responsibility in April 2013. The recommendations identified points where voluntary cooperation could smooth the process of evaluation, by sharing information and data along a coordinated, dialogue-based pathway; as well as a first draft "Transparent Value Framework".

As a follow-up, the Medicines Evaluation Committee of the European Social Insurance Platform (MEDEV) has been performing pilot projects since July 2013. Pharmaceutical companies with orphan medicines at any stage of development were invited to participate, with the objective of testing the different elements in the recommendations.

At least 15 companies have participated in the MoCA pilot projects (information as of 2018). The pilots are based on voluntary participation of all participants, and thus, there are no set procedures, and timelines vary from pilot to pilot.

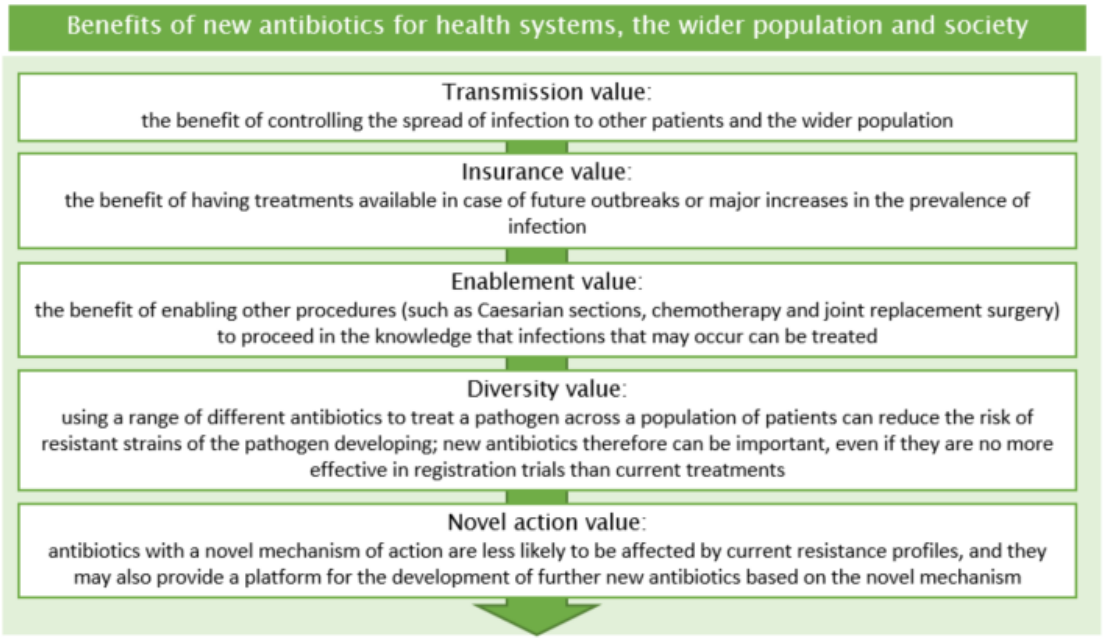
Source: example of a proposed Transparent Value Framework [54], further sources: [53, 165]

Important lessons were learned from **adaptations of the HTA methodology for orphan medicines**. Through several (large) projects, adaptations in HTA for orphan medicines have been developed (e.g. use of the MCDA methodology) [166-168]. The Medicines Evaluation Committee of the European Social Insurance Platform (MEDEV) has been performing pilots with the pharmaceutical industry to test and pilot the Transparent Value Framework (TVF) that had been created to structure a discussion about the value of new orphan medicines (cf. Box 4.2). Adapted frameworks for HTA have also been developed for oncology medicines (and for orphan medicines with oncology indications).

The adaptation of HTA methods "to evaluate the added value of such new technologies and economic analysis to understand the costs and benefits of different investments to fight AMR are needed to provide an evidence base for the uptake of interventions in the healthcare system and services" has also been demanded in the EU Action Plan, in line with a stronger involvement of

HTA bodies in AMR-related discussions [2]. A modification of the HTA methodology was also one of the key suggestions of the DRIVE AB project (cf. chapter 1.2).

Figure 4.4:
Discussion – Benefits of novel antibiotics for possible consideration in an adapted HTA framework



Source: [47, 169], presentation: GÖ FP

Models to **adapt the HTA methodology for HTA for novel antibiotics** have already been proposed [44, 46–49, 52, 170, 171]. Figure 4.4 presents an overview of "value components" that might be considered in an adapted HTA for antibiotics.

In 2019, academics published a concept of a Value of Diagnostics Information (VODI) framework [172], which proposed several dimensions for assessing diagnostics (cf. Figure 4.5). Furthermore, **assessing the value of a diagnostic** is currently being addressed in the IMI project VALUE Dx (cf. chapter 1.1).

Figure 4.5:
Discussion – Dimensions of the proposed Value for Diagnostics Information (VODI) framework

Clinical benefit / Patient empowerment » "Value of knowing and deciding" » "Planning value" » Value of "rule-out" test » "Option value"	**Operational efficiencies** » Turnaround time » Operational costs » Quality (reliability, reproducibility)
Economic efficiencies » Patient triage » Waiting time » (Re-)hospitalisation » Avoided cost of disease progression » Avoided adverse events » Shift to community care **Public health benefit** » Identification of notifiable disease allowing to take measures to contain the spread of infection	**Patient management** » Facilitate rapid, appropriate clinical management » Reduce unnecessary or ineffective testing » Manage patient expectations regarding prognosis and treatment course » Monitor condition and provide intervention

Source: [172]

4.2.2.2 Add-on funding

The study identified examples of two different types of add-on funding schemes in the study countries:

» Dedicated budgets for defined health technologies and

» Additional funding for individual reimbursement of health technologies originally included in a bundled funding system

In the case study countries, the so-called innovation funds in Italy (one oncology innovation fund and one non-oncology innovation fund, allocated with € 500 million each) were identified as examples for the first type. Beyond the study countries, there is the Cancer Drug Fund (CDF) in England (Box 4.3).

Dedicated funds are a way to privilege defined health technologies to which policy-makers would like to give priority. They are usually designed (e.g. the funds in England and Italy) so that they do not take the normal pathway through the system. But they tend to allow abbreviated and **faster access** to publicly funded health technologies **without having to meet usual requirements** such as an HTA (e.g. in the beginning of the CDF, oncology medicines which were not considered cost-effective by NICE were still funded).

Box 4.3:
Discussion – Cancer Drug Fund in England

Cancer Drug Fund (CDF): additional funding for cancer medicines without proof of cost-effectiveness

The Cancer Drug Fund in England, introduced in October 2010, aimed to provide patients access to cancer medicines that the doctors recommended but would not be funded in the NHS. The non-funding status either resulted from a negative outcome of the HTA performed by the National Institute of Health and Care Excellence (NICE; England's HTA agency) or from the fact that these medicines had not yet been subject to an evaluation.

Initially, the CDF was budgeted with GBP 50 million (€ 63 million) for 2010. But spending exceeded that amount and rose to over GBP 200 million (€ 250 million) in 2013-2014. The CDF had originally been implemented as a temporary measure until the implementation of the planned value-based pricing (VBP) system in 2014. However, the system was not introduced (while England has a pricing policy framework based on strong VBP elements, the plan had provided for a fully-fledged VBP system, see also chapter 4.2.3.1). In 2014, the CDF was prolonged, and in 2016, it was reformed following severe criticism for the absence of proof of value of the medicines funded. The CDF was changed into a "managed access" mechanism which funds cancer medicines for a maximum period of two years. During this time, they have to undergo an HTA by NICE.

Source: [81-83, 173-176]

The CDF experience suggests that dedicated budgets for defined health technologies might **weaken the "steering control" of policy-makers**, since common shaping and control mechanisms (e.g. decision-making based on HTA) could be undermined. If eligibility conditions are rather broad and cost-effectiveness is not a criterion, more and more health technologies could find their way into such a fund, and this would challenge the financial base of the fund [63]. As also seen for the CDF, **funding is likely to increase** over time. In absence of an evaluation, MAH might be incentivised to charge higher prices [176], which could be an unintended effect. There might also be **equity issues**, as patients who are in need of treatment financed through the fund in autumn might need to wait some further weeks and months until the beginning of the next year when the fund is filled again. Again, for the CDF, research did not identify an increase in inequity of access to cancer medicines by socioeconomic status but there were indications that women and older people may have had reduced access to the fund [83]. A major disadvantage of dedicated budgets is that they are a kind of separate funding tool not well connected to other policies. As such, they are considered as a key instrument to contributing to the "**budget silo** mentality" [177], which should be overcome.

While dedicated funds offer benefits to MAH and suppliers of included health technologies and may be beneficial to some patients who would otherwise lack access to these medicines, policy-makers are advised to introduce these tools only with caution for the risks and disadvantages described. If implemented, transparent and clear conditions should be attached, the fund should be designed as close as possible to the "normal" system to minimise the "budget silo" effect.

Some of these reflections, in particular the need for transparent and clear rules and the risk of unlimited inclusion of health technologies, are also relevant for the second type of additional funding. This model has been labelled "**DRG carve-out**" in recent literature [88], and it is used in the context of hospital funding.

In hospitals, health technologies are usually not reimbursed individually but as part of the bundled funding of the DRG system [79]. So individual reimbursement can **encourage the uptake of** those **health technologies** that are intended to be **privileged** whereas the DRG system incentivises the use of lower-priced health technologies (e.g. in the case of comparable alternatives) on which hospitals may generate revenues. In terms of AMR, these DRG carve-outs may be a valuable policy option to incentivise hospitals to procure and use novel antibiotics, since increased costs are covered [88].

But this policy option should also be applied with caution. Clancy et al. 2020 welcomed that this measure was not introduced, as planned, in the US, as it was feared to provide some unwelcome precedence for other health technologies [178]. In France, where the "liste en sus" was originally designed as a provisional list for high-priced medicines, medicines were, however, not moved back into the DRG system as originally planned (cf. chapter 3.1.2.6). Over time, funding for this "additional list" has grown [179]. Thus, there are similar risks as described above for the add-on funding through dedicated funds.

If policy-makers aim to implement such a "DRG carve-out" policy for AMR health technologies, they are advised to link it to a robust and transparent procedure, to carefully select eligible technologies [88] and to apply similar criteria as for the decision on individual reimbursement of the health technologies in the "normal" system.

4.2.2.3 Early access schemes

Seven of the ten study countries have early access schemes in place. The key rationale behind is to **facilitate faster patient access** to needed health technologies. While primarily targeted at patients, these schemes also provide an incentive for production and market entry to marketing authorisation holders and suppliers as they can gain market shares earlier. In addition, if these early access schemes are combined with favourable reimbursement and pricing decisions (e.g. being automatically granted reimbursement without any value assessment, free pricing), this offers additional benefits to manufacturers and suppliers.

However, there are similar risks as discussed above (cf. chapter 4.2.2.1) on waiving value assessments such as missing the opportunity to generate evidence. While privileges in early access schemes may be granted to suppliers for public health considerations, policy-makers are urged to consider, at least **at a later stage** (when moving from the early access scheme to "normal" market access), the implementation of standard reimbursement and pricing policies, including the performance of an HTA.

Faster market entry can also be assured by **accelerating decision-making processes on reimbursement and pricing**. Under the condition that public authorities have sufficient capacity, this measure

can be implemented rather easily. Nonetheless, it is important not to rush, since a thorough assessment and appraisal process takes time. Optimisation can be gained by **priority treatment in HTA and negotiations** [180]. In the case study countries Australia and South Korea, priority assessments and reviews are applied for defined health technologies (cf. chapter 3.1.2.3).

4.2.3 Selected pricing policy options

With regard to pricing, specific considerations are given to the concept of value-based pricing and free pricing. Price negotiations are discussed below as part of the procurement chapter on managed-entry agreements (cf. chapter 4.2.4.1).

4.2.3.1 Value-based pricing

While value-based pricing (VBP) is a commonly used term in policy debate, there is no clear definition and the concept is ambiguous.

In an OECD report [181] dedicated to VBP, two definitions were provided. In a narrow sense, VBP was defined as "[the price] that ensures that the expected health benefits [of a new technology] exceed the health predicted to be displaced elsewhere in the NHS[22], due to their additional cost" [182]. Such a VBP relies on a cost-effectiveness analysis and on the setting of an incremental cost-effectiveness ratio (ICER) beyond which a health technology is not reimbursed. In a broader sense, any policy **linking the price of a health technology to its value** (usually defined in terms of added therapeutic value, assessed through an HTA or a similar evaluation) was considered eligible to be classified [181].

The VBP concept in its narrow sense has fully integrated reimbursement and pricing policies. In Europe, this integrated policy framework has only been implemented in Sweden, where, among others, the societal perspective is taken into consideration in the decision on the reimbursement of a medicine and its price [183]. England aimed to introduce a fully-fledged VBP in 2014 but then discontinued to do so ("Value based pricing is dead." [184]). But in the broader sense of the VBP definition, England continues applying a value-considering approach in pricing and reimbursement, and this is the case for many other countries in Europe and beyond (all ten case study countries consider value components in their pricing decisions on (some) new medicines, though not all of them systematically, and at least three countries do so for defined medical devices, cf. chapter 3.2.1).

The **pharmaceutical industry** has been **promoting** the value approach since the 2000s [63]. In a study, pricing **authorities** and payers first ranked VBP high, but in a follow-up focus group discussion **hesitancy** was expressed: "In principle, it is a good idea, but …'. 'Value-based pricing seems perfect but …'" [185]. Reluctance was partially due to the failure of the introduction in

[22] The definition was developed in the context of the English National Health Service (NHS).

England, the feeling that the debate on VBP was industry-driven and the fact that VBP, given the need for HTA, is resource-intensive and requires quite some capacity [185].

With regard to transferability to AMR health technologies, the focus is put on the **broader definition**. It would not be realistic to establish a fully-fledged VBP on short notice[23] since it would require a complete change in the pricing and reimbursement system, and it can not be done solely for one group of health technologies.

Following up on the concept of VBP in the broader sense, it is linked to **possible limitations of current HTA methodologies** and the current understanding of "value" rather in terms of therapeutic than societal value. In chapter 4.2.2.1 these considerations were discussed in detail. Overall, a value-considering approach in pricing, resulting in higher prices of AMR health technologies based on the acknowledgement of their societal value, could be a pathway. But clear rules on the definition of societal value as well as eligible health technologies for which these privileges are granted is needed.

4.2.3.2 Free pricing

The **rationale of price regulation** is to contribute to patient access to health technologies by ensuring that the health technology is **affordable** to those who pay for it (patient or third party payer). In advanced health systems, many health technologies, in particular medicines, are funded by public payers, and this explains why several countries decided to only regulate the prices of those health technologies for which they pay (this is also a common understanding in the EU [186]). Regulating the prices of all health technologies, including those which are fully paid out-of-pocket by the patients, is based on the idea to protect patients from excessive prices.

Allowing free pricing, including the possibility to set high prices, without any funding support is per se not an incentive for private actors. Manufacturers and suppliers aim to sell their products at high prices. This can be either achieved through settings in which the suppliers are free to decide on the price (free pricing; no indirect price control through procurement) or in which applied criteria in legislation or in a negotiation support higher prices. However, high prices alone do not maximise revenues. Sales volumes are needed as well. Thus, **public funding (reimbursement) is key** since it largely contributes to uptake, otherwise some high-priced medicines would never be purchased by patients.

Therefore the German pharmaceutical system AMNOG (cf. chapter 3.2.2.1) is highly beneficial to industry as it offers privileges in both pricing and reimbursement: In the first year, the MAH can determine any price and will be funded by the public payer without having to demonstrate any evidence or justification for that price.

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[23] The focus of this report is to identify and discuss policy options that are already in place in national systems and that are considered overall feasible for implementation in other countries.

The authors do not consider the **German example** as a model for AMR health technologies. It requires high public pharmaceutical expenditure which other countries cannot allow. Furthermore, in the first year (unlimited) consumption of medicines without any conditions (apart from therapeutic conditions of use as approved by the regulator during marketing authorisation) is allowed. Since control and stewardship are needed for antibiotics, other policy options which allow public payers to attach conditions (e.g. negotiations resulting in the conclusion of MEA), appear to be more appropriate for AMR health technologies.

4.2.3.3 Price and reimbursement reviews

The focus of this study was on peri-launch policies which are taken before market entry. However, the responsibility of public authorities does not end when a price of a health technology is set or the reimbursement or procurement decision has been taken (see also Figure 1.4. on the sequential way of health technologies through the system).

An appropriate implementation of reimbursement and pricing policies includes performing "regular" reimbursement and price reviews[24] to see whether, or not, given **new developments,** inclusion into reimbursement at the determined price is still in line with the requirements as defined in legislation. If not, this could lead to "delisting" (removing a health technology from reimbursement) or to a lower price. This is of relevance given the wide-spread use of external price referencing (EPR), at least as a starting pricing policy later supplemented by further policies, in the study countries and globally [187-190]. EPR incentivises MAH to first launch health technologies in countries with a high price and later in countries with a lower-price level in order to not reduce the benchmark price. There is empirical evidence on this **"strategic launch"** of MAH [84, 148, 191, 192], and evaluations on the cost-containment impact of regular price reviews exist [100].

MAH and suppliers may benefit if public authorities do not perform regular pricing and reimbursement reviews. In only one of the study countries was this possibility identified. This may be attributable to the fact that overall legislation provides for regular reviews (with defined dates) only in few European countries, while the reviews are rather performed ad-hoc [144]. While acknowledging the workload linked to reviews, the authors are nonetheless sceptical towards omission of price and reimbursement reviews. This means missing out on major opportunities for data generation and learnings. Given public health priorities for defined AMR health technologies, policymakers may still decide to reimburse and purchase a health technology at a higher price even if meanwhile review data point to comparably lower prices in the cross-country comparison. It appears preferable to deliberately deviate from the review results rather than **omitting reviews** altogether which would mean **foregoing data collection** and thus the opportunity to generate evidence.

[24] Since same mechanisms and considerations apply for price and reimbursement reviews, they are discussed jointly in this chapter.

4.2.4 Selected procurement policy options

Managed-entry agreements (and similar negotiations) and delinkage models are discussed below as policy options that governments may apply at national levels. At the end of this chapter, the potential and feasibility of cross-country collaborations in procurement (and possibly also in reimbursement and pricing) is assessed.

4.2.4.1 Managed-entry agreements

In the course of the last decade, managed-entry agreements (MEA) have increasingly been applied by several governments in high-income countries [64, 65, 68, 85, 156]. While most middle-income countries have not yet introduced MEA (also reflected in the findings for the case study countries), they are considering changes in legislation to allow its application [193].

A few countries (e.g. Italy) started earlier, and the general idea of attaching (financial) conditions to reimbursement, pricing and procurement negotiations[25] is not new and was also done in previous time (e.g. price-volume agreements). The novelty of MEA is their systematic use as a policy option to "manage the market entry" of health technologies whose inclusion into public funding and/or procurement poses major challenges to the health system. The idea of linking payment to health outcomes (in the case of the performance-based MEA) is also a novel element. Health technologies subject to an MEA are usually medicines[26] with high price tags and frequently with limited evidence of effectiveness. Due to the medicines' characteristics (e.g. small population groups in the case of orphan medicines), sufficient data could not be collected in the clinical trials; further data might only be generated upon launch (collection of real-world data / RWD). Thus, **MEA are a policy option to deal with uncertainty** [157, 194]. Given similar products' characteristics of health technologies typically under an MEA, the MEA tool appears to be an ideal policy option for AMR health technologies. To ensure stewardship, volume control could be built in as one of the conditions.

Indeed, advantages of MEA were reported from different actors (public authorities and payers, industry) since MEA were perceived to address several policy objectives and challenges (i.e. to ensure early patient access, financial sustainability and returns for industry). MEA were shown to contribute to **faster and earlier access** [195].[27]

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[25] MEA is also a policy that can be classified to the policy areas of reimbursement, pricing or procurement.

[26] MEA for medical devices are possible but not common (apart from price-volume agreements).

[27] While early access has been stated as a major benefit of MEA in several pieces of literature, to the knowledge of the authors, there is only one empirical study investigating this topic.

Table 4.3:
Discussion – Advantages and disadvantages of managed-entry agreements

Advantages	Disadvantages
Enable access to health technologies otherwise unaffordable	Fund health technologies that do not prove the added (therapeutic) value and are not cost-effective
Early access to health technologies	Need to prolong MEA in case of limited data generation
A supporting tool for financial sustainability (cost-containment)	Incentivise industry to systematically ask for higher list prices
Allow public payers to manage uncertainty (in case of limited evidence)	Have raised expectations with patients, difficulty to de-list (disinvestment policy)
Collect real-world data (performance-based MEA), expand time horizon for data collection	Are connected to large administrative efforts, resource- and time-intensive (no defined methodology / good practice)
Send signals to manufacturers on key therapeutic areas to inform R&D decisions	Send signals of payers to accept higher prices
Allow industry to do price discrimination in an environment of external price referencing	Contribute to a situation in which other countries overpay when applying external price referencing (net prices are confidential)
	Increase information asymmetry Payers are not on an equal playing field with MAH Weakens the bargaining power of payers

Source: GÖ FP based on literature [62, 68, 85, 157, 194, 196, 197]

At the same time, MEA have some disadvantages (cf. also Table 4.3). The most commonly reported ones concern the high administrative burden and issues of limited transparency.

MEA are **resource-intensive** and connected to **high administrative burden**, not only for their implementation but also regarding monitoring the performance in the case of performance-based MEA. A study evaluating the MEA in the Netherlands between 2006 and 2012 found that for one third of research questions defined at the beginning, insufficient evidence had been generated through the performed outcome research studies to reach grounded conclusions four years later [196]. Some of the data generation activities were stopped due to the high workload. It is essential that policy-makers clarify from the beginning

» what should be done if that needed **RWD** will not be generated in the time period planned (prolongation of the MEA and/or continuation of public funding?),

» if during research, the need for further RWD is discovered (modification of the MEA?) or

» if the RWD demonstrate poor health outcomes (stop public funding as foreseen in the MEA?).

The last point suggests the need for a **disinvestment strategy**. Important ethical issues also come into play: what does it mean for patients who hope for a successful treatment when they learn about the poor outcomes of the health technology? The evaluation on the MEA in the Netherlands found that after the four years reimbursement was continued for half of the medicines based on further evidence generation to address remaining uncertainties. While acknowledging conditional funding (i.e. the MEA investigated in the Dutch study) to be a quick but conditional access to medicines "theoretically", the authors of that study pointed to numerous aspects related to the MEA's design and implementation that negatively affected their value in practice [196].

Transparency issues are linked to the wide-spread practice of external price referencing (**EPR**) globally [64, 65, 84], which is frequently used as the first policy option to set prices of health technologies. Since the benchmark price determined through EPR is frequently not affordable for payers, they then enter into negotiations with the MAH which frequently results in the conclusion of an MEA, with a confidential deal, including a secret negotiated price. In the current business model, confidential prices are important for the industry, since it will be again the list prices that are communicated and serve as indication for further countries that will also apply EPR (and, in the following, conclude MEA), cf. Figure 4.6.

One of the arguments in favour of confidential discounts is that it allows industry to **price-discriminate** (i.e. offer different (real) prices to different countries). So lower-resourced countries could be granted lower (real) prices (while keeping higher list prices to be used in EPR) and have access to health technologies [198]. The validity of this argument can neither be confirmed nor rejected because due to the confidentiality of data only few studies in this area were performed [197, 199]. One of the very few studies performed on net prices does not confirm the stated benefits of confidentiality: The study identified comparably high discounts for oncology medicines in the high-volume markets of Italy and also Spain, whereas for the same products, no discounts were offered or these medicines were not all marketed in some Central and Eastern European countries [200]. In addition, economic theory suggests that the **discounts have been built into the official list price**. The latter was confirmed in an empirical study (at least 5% higher list prices for medicines subject to a MEA) [201]. Furthermore, strategic negotiation considerations challenge possible benefits of confidentiality: purchasers (public payers) are not on a level playing field with the MAH, and the existing information asymmetry in the area (cf. chapter 1.3.1) increased.

Figure 4.6:
Discussion – Interlinkage between external price referencing and managed-entry agreements

Source: GÖ FP based on literature [84, 157, 197]

In response, at international level, initiatives to improve the transparency in the markets of health technologies have been launched. A milestone in this respect is the Resolution "Improving the transparency of markets for medicines, vaccines, and other health products" of the World Health Assembly (WHA) from May 2019 [202] requesting the WHO and Member States to launch appropriate action. The **WHA Resolution** explicitly mentioned the WHO "Fair Pricing Initiative" which explores new business models to ensure access to new medicines (including those with high price tags and limited evidence), and in this respect, improving transparency is a major aspect [203]. As a follow-up action on the WHA Resolution, the "Oslo Medicines Initiative" was initiated by the government of Norway in collaboration with the Regional Office for Europe of the WHO. This initiative explores further pathways to improve transparency: while acknowledging that for single countries it is difficult or practically impossible to step out and request transparency, new models of collaborative approaches of countries, in dialogue with the industry, are explored [204]. This links to the opportunities resulting from, and need for, cross-country collaboration in reimbursement, pricing and procurement of health technologies, even if the policies per se remain national ones.

Despite their disadvantages, MEA still appear to be appropriate policy options to address the challenges of AMR health technologies. However, if applied, it should be ensured to "do it right" as far as possible. However, no policy guidance document or checklist on how to best design and implement MEA is available, also because this policy option has been developed over the years during its application. But experience of countries allows cross-learnings, and academics [205, 206] as well as international organisations such as OECD [157] published principles to consider when implementing MEA.

In addition to aiming for transparency in MEA, if possible, policy-makers opting for the implementation of MEA for AMR health technologies should consider designing them by inclusion of "delinkage" mechanisms (cf. below chapter 4.2.4.2).

4.2.4.2 Delinkage models

The concept of delinkage has been discussed for more than two decades in pharmaceutical policy debate. In general, it relates to delinking the revenue for the MAH, or the price, from the cost for R&D [207-209]. This is based on industry arguments that they require to recoup their investment into R&D or into a purchase of a start-up enterprise.

Box 4.4:
Discussion – Contracts with delinkage to volumes for novel antibiotics in Sweden and UK

Sweden – Pilot on procurement contracts offering an annual revenue guarantee to antibiotic manufacturers

Since 2018, Sweden has been piloting a model in that suppliers of new antibiotics are granted an annual revenue guarantee. It particularly targets antibiotics with low volume, for which the Swedish market might likely become unattractive. In early 2020, the Swedish Public Health Agency launched an open procurement call and invited MAH to submit candidate medicines for the pilot (i.e. antibiotics with efficacy against a pathogen in the "Priority 1 Critical group of the WHO Priority Pathogen List" and with acceptable safety profile). In July 2020, contracts with five antibiotic suppliers were concluded for a period of two years. The "guaranteed annual revenue" was set for each selected antibiotic, based on the cost of a "security stock" (reserve amount) at 50% above the average European list price.

Swedish hospitals continue to purchase as normal with the funding from the pilot study paying the difference between the guarantee and actual sales. If, in case of unexpectedly large sales volumes, the guaranteed annual revenue were exceeded, a bonus corresponding to the price of purchasing 10% of the "security stock" would be paid.

UK – Pilot on fixed annual subscription fee for market entry and supply of a novel antibiotic

The UK government is piloting a similar model called "the commercial model" in England. This model is based on the concept that manufacturers will be paid a fixed annual fee for the supply of an unlimited amount of the antibiotics (as much as needed). The outcomes of an HTA performed by NICE will impact the amount of the annual subscription fee which will be up to GBP 10 million per product. Given the limitations of traditional HTA in assessing novel antibiotics, a new cost-effectiveness evaluation methodology specific to new antibiotics is being developed. The target implementation date is early 2022: initial contracts will be for three years, with an option to extent to ten years.

Source: [5, 88]

Models explored in the study, however, relate to delinkage from the volume consumed, i.e. a kind of subscription model. Among the study countries, only Australia was found to apply such a model. It has been designed as a subscription model (also nominated as "Netflix" or "All-you-can-treat" model). The Australian government, which aims to eliminate hepatitis C by 2030, concluded agreements with five manufacturers of hepatitis C medicines and offered a fixed revenue for treating an unlimited number of patients with hepatitis C medications with in a period of five years (cf. chapter 3.3.2.4).

In Sweden and UK, such delinkage contracts have been implemented on a pilot basis for antibiotics (cf. Box 4.4).

This delinkage models are, in particular, of interest for antibiotics for which volume is to be controlled to avoid AMR. They "break" the normal business rationale of increasing revenue by increasing volume. There are again different ways to design them. It has been argued that the design of the UK pilot models corresponds rather to an MER [88].

Delinkage models appear to be less a policy of its own, but they are important components of the implementation of procurement contracts. In addition, they can be combined with other specific policy elements (e.g. adapted HTA), as the UK example shows.

4.2.4.3 Pooled procurement and cross-country collaborations

In order to increase volumes and thus bargaining power, pooled procurements have been performed in the study countries. As described in chapter 3.3.2.5, the levels of pooling differ: collaboration of hospitals (e.g. hospital groups), joint procurement at regional level or – for some or all health technologies – at federal level. Some non-study countries in Europe (e.g. Denmark, Norway) have established centralised procurement agencies to serve all public hospitals with medicines and medical devices [18, 118].

Pooling public procurements appears to be a valuable policy option for AMR health technologies, in particular antibiotics, since it can **address the challenge of low and fragmented volumes** (cf. also Table 4.2). However, it is important to do procurement right.

Public procurement is, in general, **challenging**, and public procurers have experienced failures. New procurement tools can be helpful, such as the MEAT principle (to consider value), the "plural-winner" principle (to avoid monopolisation and eventually the unavailability of health technologies) and the DPS (to offer flexibility) as presented in chapter 3.3.2.5. Despite the benefits of pooled procurement [210], it is common knowledge that with increased aggregation the system becomes more complex and thus prone to failures. Even the introduction of centralised procurement of health technologies is not easy. It is key to have well-aligned procedures, clear rules and standard operating procedures, to ensure close communication with the "users" (e.g. hospitals) and stakeholders (suppliers) and to have strong governance and monitoring systems [18, 118, 210]. An evaluation of the Portuguese centralised procurement for medicines has also pointed to the importance of good collaboration between hospital pharmacists with clinical expertise on medicines and procurement experts of the procurement agency [118]. Since AMR health technologies are also very specific, this is a major learning as well.

Box 4.5:
Discussion – Experience of joint procurement in cross-country collaborations in Europe

Baltic Procurement Initiative – successful joint procurements on vaccines

In 2012, a partnership agreement on joint procurement between the three Baltic countries Estonia, Latvia and Lithuania was signed. For practical reasons, the initiative has focused on the joint procurement of vaccines but an extension to other medicines is possible.

For each procurement, one of the countries is nominated as a lead partner who is mandated by the others to carry out the procurement on their behalf, in line with its national legislation. Lead partners differ per procurement, and not always all three partners are involved (depending on whether, or not, the vaccine to be procured is in the respective national vaccination schedule).

The first joint procurement for the bacille Calmette-Guerin vaccine in 2015 failed due to supply shortage. Thereafter, the Baltic Procurement Initiative undertook three successful joint procurements of vaccines.

Major learnings include:

» The lead partner has a major role and responsibility.
» In the beginning, solutions to overcome differences in organisational and legal procedures have to be sought.
» Over time, with experience, the preparation and management of procurement procedures got easier.
» Clarity of the procurement procedures is considered key. Short and simple procurement documents have developed into good practice.
» Rotation of the lead partners proved to be useful.
» Since the engagement for the initiative was voluntary, it is add-on work for the involved technical experts. This was a limiting factor, particularly in the beginning.
» Market feasibility analysis, including market research with possible bidders, is seen as a key prerequisite.
» Political support and the interest of policy-makers in the progress made by the technical experts is important.

Nordic Pharmaceutical Forum – conclusion of a first joint Nordic tender

In 2015, under the lead of the Danish central procurement agency AMGROS, Denmark, Norway, Sweden, Iceland and Finland as an observer, started to collaborate in the areas of horizon scanning, security of supply, joint procurement and price negotiations.

At the end of 2019, the collaboration successfully concluded the first joint tender. The focus of this initiative is not only on new medicines, but also on older hospital medicines that have increasingly been in short supply. For the first Nordic tender, the collaboration identified the six most undersupplied older hospital medicines. In September 2018, the procedures started with a meeting with possible bidders to do market research. Overall, the Nordic tender was characterised by a strong stakeholder involvement. Before publishing the call for the tender, the collaboration conducted hearings with potential bidders for six weeks and then revised the tender call documents.

Major learnings include:

» The extensive dialogue with possible suppliers is considered a key success factor.
» Legal barriers are challenging and may prevent participation of some countries.
» Collaboration is easier for countries with similar health and pharmaceutical systems.
» Sufficient resources for preparing and performing a tender are required.
» Efficient and timely planning, including on logistic aspects, is key.

Source: [159]

Alongside the challenge of centralised procurement in a single country, **cross-country joint procurements are even more complex**. But if they are successful (and this is possible), they are **rewarding**. In recent times, cross-country collaborations in procurement that are organised and led by countries[28] have been on the rise. In Europe, these include the Baltic Procurement Initiative, the Nordic Pharmaceutical Forum, the Valletta Declaration (involving some study countries) and Fair and Affordable Pricing (FAAP).[29] The first two have already successfully concluded joint procurements (see Box 4.5), while the two others are still in the planning phase. A major challenge which they meet is limited interest of suppliers to interact with a collaboration [159].

The challenges of pooled procurement within a country are intensified in cross-country collaborations. In particular, collaboration in procurement of countries with differences in the organisation of the health system proves difficult. Involvement of countries with fragmented health systems into cross-country procurement can be demanding. Legal and also language barriers were reported [159].

While cross-country procurement (without any coordinating structure provided by an international or interregional organisation) definitively has value and could also be considered for AMR health technologies, it appears to be a **solution in the longer run**. Before engaging in cross-country procurements, pooled procurement at national level should be fostered. This allows preparing the system for cross-country cooperation and also to have first lessons learned.

The benefits of cross-country collaborations are not short-term. While the authors advise sufficient preparation before moving forward with joint procurements by several countries, there is a lot to gain from **cross-country collaboration in other areas**, including sharing of information and experience. In fact, the above-mentioned cross-country collaborations also aim to work together in other fields, mainly HTA and horizon scanning.

[28] i.e., without any interregional coordinating structure, as it is the case for the three procurement collaborations (PAHO Revolving Fund and EU procurements on medical countermeasures described in chapter 3.3.2.5.

[29] The Beneluxa Initiative does not aim to perform joint procurement. Its members collaborate in some other areas, including in horizon scanning, HTA and joint pricing and reimbursement negotiations. In literature, the Beneluxa Initiative is sometimes wrongfully referred to a procurement collaboration.

4.3 Pathways for the future

The analysis of identified examples in the case study countries and in further countries suggests that some specific reimbursement, pricing and procurement policies appear to have the potential to incentivise the market entry and uptake of AMR health technologies.

Promising models include

» **adapted value assessment frameworks** (HTA) that take into account the societal value and special characteristics of AMR health technologies and may eventually allow inclusion in reimbursement despite absence of data and evidence in terms of added therapeutic benefit and
» **managed-entry agreements** or similar procurement contracts that have AMR relevant conditions (e.g. good stewardship, environmentally friendly) and may be designed to carry a **"de-linkage model"** (payments independent from the sales volume).

However, both measures (adapted HTA and MEA) come at a cost, at least in the short term. Even if in the long run these measures may pay off from a public health perspective, public authorities have to invest first.

At several points, the study has shown the strong interlinkage between reimbursement, pricing and procurement. For a marketing authorisation holder or supplier, premium prices are not an incentive to market if there are no purchasers (e.g. no reimbursement). As a result, policy-makers are advised to opt for measures that consider both aspects (price and volume, to ensure sufficient revenue; or in case of controlled consumption of antibiotics, a revenue to compensate for lower volumes). The two above-mentioned policy options have such multi-tier approaches.[30] Overall, policy-makers are advised not to focus on a single measure but to move toward by **implementing a well-aligned combination of policy options**. As a rule, specific reimbursement policies appear to particularly address the challenge of AMR health technologies regarding their limited evidence, while specific pricing policies address the challenge of low prices and specific procurement policies address the uncertainty regarding sales (and revenues) (cf. Table 4.2).

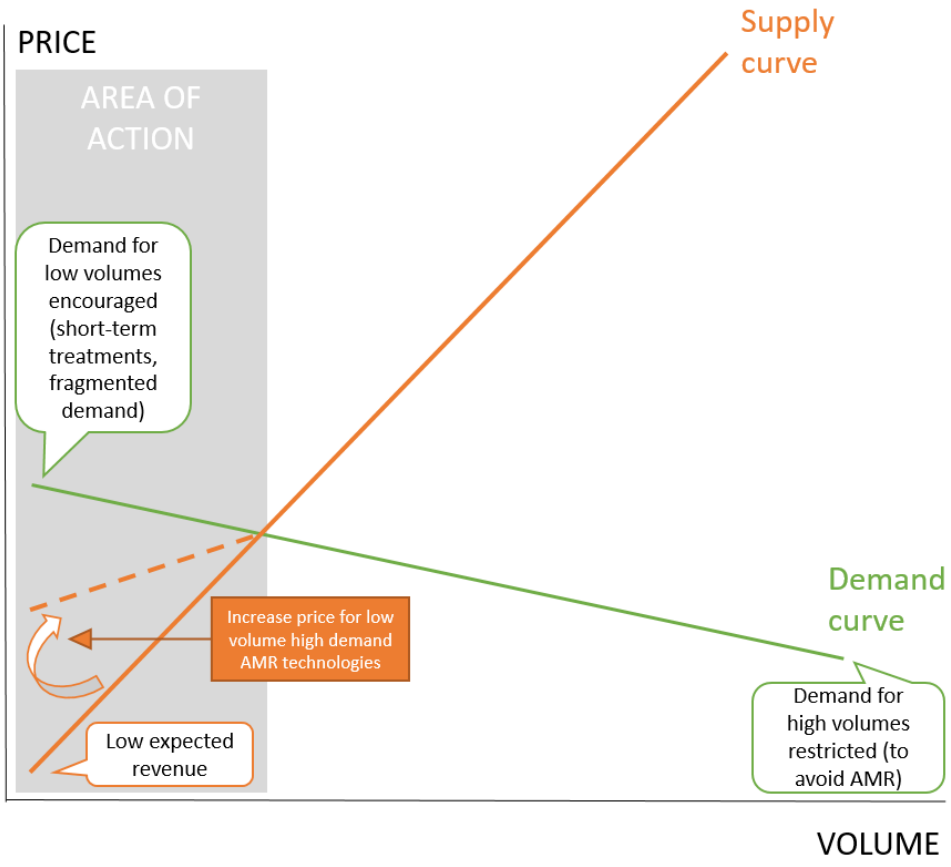
Despite some interesting models identified in this study, the **area for action is limited**. As the macroeconomic model in Figure 4.7 visualises, the area for action is just where demand exceeds supply. In these cases, exemptions from, adaptions of and additions to standard policies that justify higher (reimbursement) prices, public funding or procurement for the health system despite limited evidence are possible.

The study identified considerably **fewer examples** of specific policy options **for middle-income countries** (among the study countries and in general in the literature) compared to high-income countries **and for medical devices**, including diagnostics, compared to medicines. This is likely

[30] Adapted HTA allow inclusion in reimbursement, thus public funding and possibly higher prices. Procurement contracts with delinkage also ensure funding by the public payer and thus uptake and sufficient revenue even in case of low volume.

attributable to the fact that overall in **middle-income countries** and for **diagnostics** the extent of regulation (in terms of safety and quality) and policy implementation (reimbursement and pricing) is lower [57–60]. Thus, deviations from the standard policies are also fewer. This does not exclude **transferability** to middle-income countries and to diagnostics, but policy implementation, though possible in theory, might be more challenging in practice. In some cases, policies cannot be implemented. For instance, how to develop a specific value assessment that considers and quantifies different aspects of societal value if no "traditional" HTA has yet been introduced?

Figure 4.7:
Discussion – Macroeconomic model on the area of action for AMR health technologies



Source: GÖ FP

In applying policy options identified in this study, their possible implementation in other countries should be guided by acknowledging that there is **no "one-size-fits-all-solution".** Thus, it is of uppermost importance to consider two major principles in the development and implementation of national policies:

» **Country context:** Any policy implementation must take into account the specificities of the national policy framework. Health and pharmaceutical systems vary across countries due to differences in overall policy objectives (e.g. public health versus industry focus, legislation,

organisation and funding, role of stakeholders and "culture" aspects). What works well in one country may result in a failure in another country. Thus, policy-makers are urged not to do "copy-pasting" of policy measures but rather benefit from strategic bench-learning among countries as a basis for national policy-making.

» **Monitoring and evaluation:** Even if a policy is successful in achieving intended policy objectives, its effectiveness may "fade out" after some time since market actors have adapted and/or situations have changed [69]. Thus, it is key to ensure regular monitoring and evaluation of policy measures and adaptions if necessary (see also chapter 4.2.3.3). For AMR health technologies with limited evidence, evaluations are particularly important since data collection in "real life" over time may offer further insights.

Caution should be taken related to those policies in which **policy-makers** leave the **"driving seat",** such as **free pricing or exemptions** (e.g. exemption from HTA or other evaluations). It is the responsibility of policy-makers to provide strategic guidance. In addition, exemptions from assessments imply missing opportunities to generate data. Furthermore, research and policy evidence have shown dangers of simply "pumping" money into the system to privilege defined health technologies (through separate funds), in particular without any conditions attached (such as linking to the outcome of an HTA). A drawback of such "budget silo" funds is that they have been established outside the "standard" system and are not well connected. An exemption to consider, however, is additional funding for innovative health technologies by individually reimbursing them in a hospital setting (**"carving out" of the DRG** system). However, clear and transparent criteria (eligibility), rules (when to "carve out" and when to move back to the DRG system) and conditions (stewardship) are needed if this specific policy option will be implemented.

There is a common understanding that new ways to tackle AMR are needed. Though political will and investments are required, **countries** benefit from not having to start from scratch. They **can build on existing national policies** that have been tested and implemented for other health technologies of high societal value in some countries. Though caution has to be taken with regard to transferability, these policies can be used as a blueprint.

It must be remembered that the decision of the choice of the policy mix is with the policy-makers, and it is a **political**, not a technical **decision**. Policies, mechanisms and tools to measure and assess value and to develop payment models and purchase contracts that acknowledge value are to a large extent available and can be further adapted by technical experts. But policy-makers have to decide if they acknowledge and remunerate the concept of "value", including societal value. Some authority representatives have voiced concern that a "value-based" policy is an "industry measure" [185].

The study also found value in cross-country collaborations. Due to the novelty of some of these collaborations, results are missing (e.g. no joint procurement performed up to now). **Cross-country collaborations** are to be considered as a possible avenue but challenges due to legal barriers and differences in the organisation of health systems remain. Collaboration on methodology work (e.g. on HTA methods) is easier while cross-country collaboration in reimbursement, pricing and procurement have to address the challenge of aligning different legislative procedures and rules.

The study did not identify any example of specific policy options that addressed the "pair" of an antibiotic and companion diagnostic tests. Possible reasons might include the general lack of specific policy options for diagnostics, different suppliers offering the antibiotics and the diagnostics as well as the fragmentation in several health care systems. From other areas (e.g. oncology medicines), policies addressing both oncology medicines and the companion diagnostics as part of a personalised medicine approach are known [211].

It can be beneficial to reflect on **developing specific policy options for these "pairs" in the long run.** This, however, requires a collaboration between the suppliers of the antibiotic and the diagnostics (or production of both by the same manufacturer). This also addresses different technology areas for which, as shown for study countries, currently different policies might be in place. It is a challenge, but still worthwhile to consider.

The EU Action Plan on AMR [2] has called for a stronger involvement of HTA bodies in AMR-related discussions. This study suggests that the two "worlds" of the "AMR community" and the "pricing and reimbursement community" exist in parallel: Policy-options based on similar concepts are addressed under different names in the two worlds, and without taking reference to the discussion in the other community, for instance. A **broader collaboration of the experts of both communities** would be highly beneficial. This study aims to provide a contribution to support such a collaborative approach.

5 Conclusions

AMR health technologies include novel antibiotics and (rapid) diagnostic tests that offer high value to society (societal value), as they contribute to population health by tackling AMR. At the same time, AMR health technologies face specific challenges such as absence of data and evidence (resulting in the difficulty to demonstrate their value), low prices, low fragmented volumes (difficulty to generate sufficient revenue) and limited "planning certainty".

Over the years, national governments have implemented reimbursement, pricing and procurement policies to ensure access to (essential) health technologies for their population while aiming to maintain the sustainability of their health systems. Based on defined tools and criteria, decisions on inclusion of health technologies in the public benefits package scheme are taken, and prices of health technologies – usually those that are paid by public payers – are regulated. Specific procurement contracts (e.g. managed-entry agreements) have been concluded between public payers and suppliers to allow access to health technologies despite high price tags and limited evidence of their therapeutic benefit.

The rationale behind pricing and reimbursement policies is that – in line with clinical guidelines on use – access to therapeutically necessary health technologies should be provided to patients at a price that the system and the patient can afford. Within the boundaries of appropriate use, the aim is to contribute to **improved access** to cover all patients who need the medication. Limiting use (as for antibiotics to avoid negative externalities such as AMR) is normally not the intention when ensuring access to health technologies. Cost-effectiveness analysis remains a guiding principle in pricing and reimbursement decisions of health technologies. Thus, new health technologies either have to demonstrate an added therapeutic benefit in comparison to comparators or an economic advantage (i.e. a lower price). Health technology assessments (HTA) that are performed to inform price and reimbursement decisions tend to not capture the societal value.

Specific policy options have been implemented to ensure the market entry and uptake of health technologies with similar specificities as AMR health technologies: Such policies in reimbursement, pricing and procurement were identified in particular for orphan medicines and for specific indications such as cancer. A few countries have implemented policies to promote the commercialisation of novel antibiotics and to reward antibiotic manufacturers. Significantly fewer specific policies were reported for medical devices, including diagnostics, but this may be attributable to the lower level of regulation and policy implementation for these health technologies in general. More specific policy options were found in high-income countries which have overall a broader range of measures in place.

The identified specific policy options in this study can be categorised into exemptions (from cost-containment), modifications (of existing methods and policies) and additions (additional funding). Examples of exemptions include free pricing on behalf of suppliers (i.e. exemptions from price regulation as it is the case for most medical devices and non-reimbursable medicines in most study countries), no claw-backs and discounts (e.g. for orphan medicines and generics in some countries) and exemption from an HTA (for antibiotics addressing AMR in Germany). Modifications

that were identified to exist include higher prices (premium prices) granted and/or higher reimbursement rates for specific medicines groups, application of new procurement tools ("Most Economically Advantageous Tender" criterion) and purchasing contracts (e.g. delinkage model for hepatitis C medication in Australia and managed-entry agreements in most study countries). Additional funding sources were found to have been made available for orphan and cancer medicines (e.g. specific funds) and for defined medicines in hospitals on top of the diagnosis-related groups system (e.g. France, Germany).

The examples identified in the study countries and further countries show that several policies are already in place and have successfully passed the proof of concept. These policy options may thus serve as models for consideration of possible adaptions and implementation for incentivising development and market entry of AMR health technologies.

For application to AMR health technologies, most **promising models appear to adapt the HTA methodology** (value assessment framework), by taking into account the societal value and special characteristics of AMR health technologies, **and conclude managed-entry agreements with** appropriate **conditions attached, including possibly a delinkage model**. Under certain conditions, **individual reimbursement** of AMR health technologies used in hospitals **on top of DRG funding** could be another option. Joint procurement helps to increase volumes and strengthen bargaining power.

While the tools are available and can be used and further developed by technical experts, it is, however, a **political decision of the policy-makers** if they are willing **to acknowledge the societal value** of AMR health technologies or if they prefer a narrower approach by rewarding mainly added therapeutic benefit.

Overall, this tool box of policy options should be used with caution, taking into consideration country-specific characteristics and specificities of AMR health technologies (e.g. linking incentives to appropriate antibiotic stewardship). No simple "copy-paste" of policies from one country to another and from one specific health technology to another should be done.

In addition to examining transferability of policy options in their national contexts, countries are also urged to consider the financial implications of the policy implementation, since – independently from their design as exemption, modifications or addition – incentives to encourage development, production and use of AMR health technologies are linked to investments.

While the specific policy options benefit from having been tested for other health technologies and can be adapted on short notice, more long-term solutions could also be explored. One approach is to benefit from cross-country collaborations (e.g. pooled procurements), but is not realistic in the absence of a coordinating structure organised by an international institution or a lead country. Successful implementation requires sufficient preparation, also in terms of aligning procedures and legislation. In addition, thought could be given to **novel funding mechanisms that jointly address the "pair" of the antibiotic and the diagnostic tests as its "companion"**.

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7 Annex

7.1 Additional information regarding methodology

7.1.1 Key data of the case study countries

The ten selected countries vary with regard to general characteristics in terms of geography, demography and income group as well as with regard to specificities of the health care system, and health spending and the pharmaceutical market, including its size.

In the main body of the study, Table 2.1 provides an overview of key data of the study countries.

The population size in the ten selected countries ranges from 25 million (Australia) to 211 million (Brazil) inhabitants. The country with lowest total GDP in the group is South Africa with 351 billion USD in 2019, whereas the country with the highest GDP is Germany with 3,846 billion USD. There are also differences in current health expenditure as a percentage of the GDP. Germany and France spend around 11% of their GDP on health (2019) while Saudi Arabia (around 5%) and Turkey (around 4%) spend a lower percentage of their GDP on health care financing. An important indicator for understanding health systems is the share between public and private financing. For example, Brazil (for which results in the study are mostly only available for the public sector) has a comparably high proportion of private health expenditure of nearly 60%. France, Germany, Italy, Spain and Turkey show lower percentages of private health expenditure ranging between 20% and 30% of the total health expenditure. The shares of total (i.e. public and private) expenditure for medicines as a percentage of total health expenditure ranges from Turkey (nearly 30%) to Brazil (less than 10). Data on spending for medical devices is not available.

To approximate the importance of the countries as a market for antibiotic products, figures on antibiotic consumption are included in Table 2.1.[31] The highest antibiotic consumption is in Turkey (around 38 DDD per 1,000 inhabitants per day), followed by South Korea (around 28 DDD per 1,000 inhabitants per day). Germany, with 11.5 DDD per 1,000 inhabitants per day, has the lowest antibiotic consumption of the countries included in the study and it is around three times lower than in Turkey.

[31] There are two aspects to consider: On the one hand, higher antibiotic consumption reflects the market size of a country for antibiotic technologies. On the other side, higher antibiotic consumption may suggest higher AMR.

7.1.2 Literature review

It was not expected that the literature would provide in-depth information on specific policies. The authors have access to an extensive network of experts in the field of purchasing/pricing and reimbursement policies for medicines and also medical devices from many countries (including representatives of the Pharmaceutical Pricing and Reimbursement Information / PPRI nework). The literature review therefore was of minor importance to this study. Still, an intitial literature review for the 10 countries selected was performed with the aim to pre-fill country fact sheets and was primarily based on unsystematic hand searches of grey literature. The rationale behind this decision was the experience from previous work that such policies, in particular if related to concrete examples are rarely published in peer-reviewed literature. If published, literature in the field usually relates to only a few large high-income countries. In addition, publication delay is common, which is an issue for this study given the aim of identifying up-to-date novel solutions. Furthermore, a systematic literature review (with strict eligibility criteria) was considered to be too limited for the scope of this study.

The authors initially consulted the following websites and their internal literature archives for the identification of relevant literature and data sources. The websites were searched for grey literature and data sources on the issue of AMR, antibiotics, diagnostics and policy options in the areas of pricing, reimbursement as well as procurement.

- General literature:
  - European Union (European Commission, particularly DG SANTE, DG Research, Council of the EU, European Parliament)
  - WHO (Headquarters and Regional Offices),PAHO
  - OECD
  - The WHO Collaborating Centre for Pharmaceutical Pricing and Reimbursement Policies, including the Pharmaceutical Pricing and Reimbursement Information (PPRI) network
  - European Observatory on Health System and Policies
  - European Public Health Alliance (EPHA)
  - European Centre for Disease Prevention and Control (ECDC)
- Country search of the case study countries:
  - HTA agencies
  - Public authorities for pricing and reimbursement, public payers
  - Associations (e.g. civil society such as patient associations, industry associatiosn, health care providers)

GÖ FP also drew on its own previous and ongoing work and information partially unpublished:

» Findings of a systematic literature review on medical devices for infectious diseases,
» Findings on a systematic literature review on pricing and reimbursement policies in Europe as of 2014,
» Information collected from countries involved in the PPRI network.

7.1.3 Survey tool

Each country fact sheet consisted of 3 parts.

Flow-charts

Two simplified country flow-charts of the standard and specific policies – one for medicines including (novel) antibiotics and one of medical devices including (novel) diagnostics. The sequence of the presentation of the policy areas (reimbursement, pricing and procurement) in the flow-charts is variable depending on the country context, but the colour scheme was standardised.

Reimbursement, pricing and purchasing of antibiotics and diagnostics – standard policies

This part of the country fact sheet presents the standard policies in detail and provides for a structured approach for all countries selected. Standard procedures for antibiotics and diagnostics were presented in two columns next to each other (i.e. in the same line to facilitate identification of similarities). The standard procedures are allocated to the relevant policy area (however, the researchers acknowledge that some policies and mechanisms could be classified under other policy areas as well). Specific questions related to the inpatient sector.

Table 7.1:
Annex – Standard policy options as presented in the countries' fact sheets

Policy Area	New medicines including antibiotics		Medical devices including diagnostics	
	Standard policies	inpatient	Standard policies	inpatient
Reimbursement	Scheme		Scheme	
	Institutions		Institutions	
	Reimbursement lists and funding mechanisms		Reimbursement lists and funding mechanisms	
	Value assessment (HTA)[1]		Value assessment (HTA)[1]	
	Reimbursement rates		Reimbursement rates	
	Patient co-payments		Patient co-payments	
Pricing	Institutions		Institutions	
	Regulated price types		Regulated price types	
	Criteria to set medicine prices		Criteria to set prices of MD	
	External price referencing		External price referencing	
	Internal price referencing		Internal price referencing	
	Value-based pricing		Value-based pricing	
	Cost-plus pricing		Cost-plus pricing	

Policy Area	New medicines including antibiotics		Medical devices including diagnostics	
	Standard policies	inpatient	Standard policies	inpatient
Procurement (purchasing)	Institutions		Institutions	
	Tendering and negotiations		Tendering and negotiations	
	Conditional pricing / Managed-entry agreements		Conditional pricing / Managed-entry agreements	
	Pharmaceutical industry contributions (claw-backs)		Pharmaceutical industry contributions (claw-backs)	
	Collaboration in procurement		Collaboration in procurement	

[1] HTA was grouped under reimbursement policies, but also feeds into pricing decisions.

Source: GÖ FP

Table 7.1 presents the set-up of this part of the fact sheets that GÖ FP had provided in a pre-filled way to country experts. The fact sheets relate to medicines including (novel) antibiotics as well as medical devices including diagnostics. Where data could not be pre-filled or contradictory, experts were asked to clarify. In addition, specific questions to "dig deeper" were asked.

Exceptions and incentives across the value chain (specific policy options)

This part of the country fact sheet describes in further detail the information on exceptions and incentives presented in the flowchart(s) and provides for a structured approach for all countries selected. In line with the tender specifications, the focus was set on pricing, reimbursement and procurement policies, however, potentially relevant policies pre- or post-launch are also considered (in order to cover all potential incentives across the value chain).

The fact sheet contained questions regarding specific policies in the respective countries for both antibiotics and diagnostics requesting also information on specific policies potentially applicable to novel antibiotics and diagnostics from other medicines, other health technologies and other policy areas.

7.2 Background information of the study countries

7.2.1 Australia

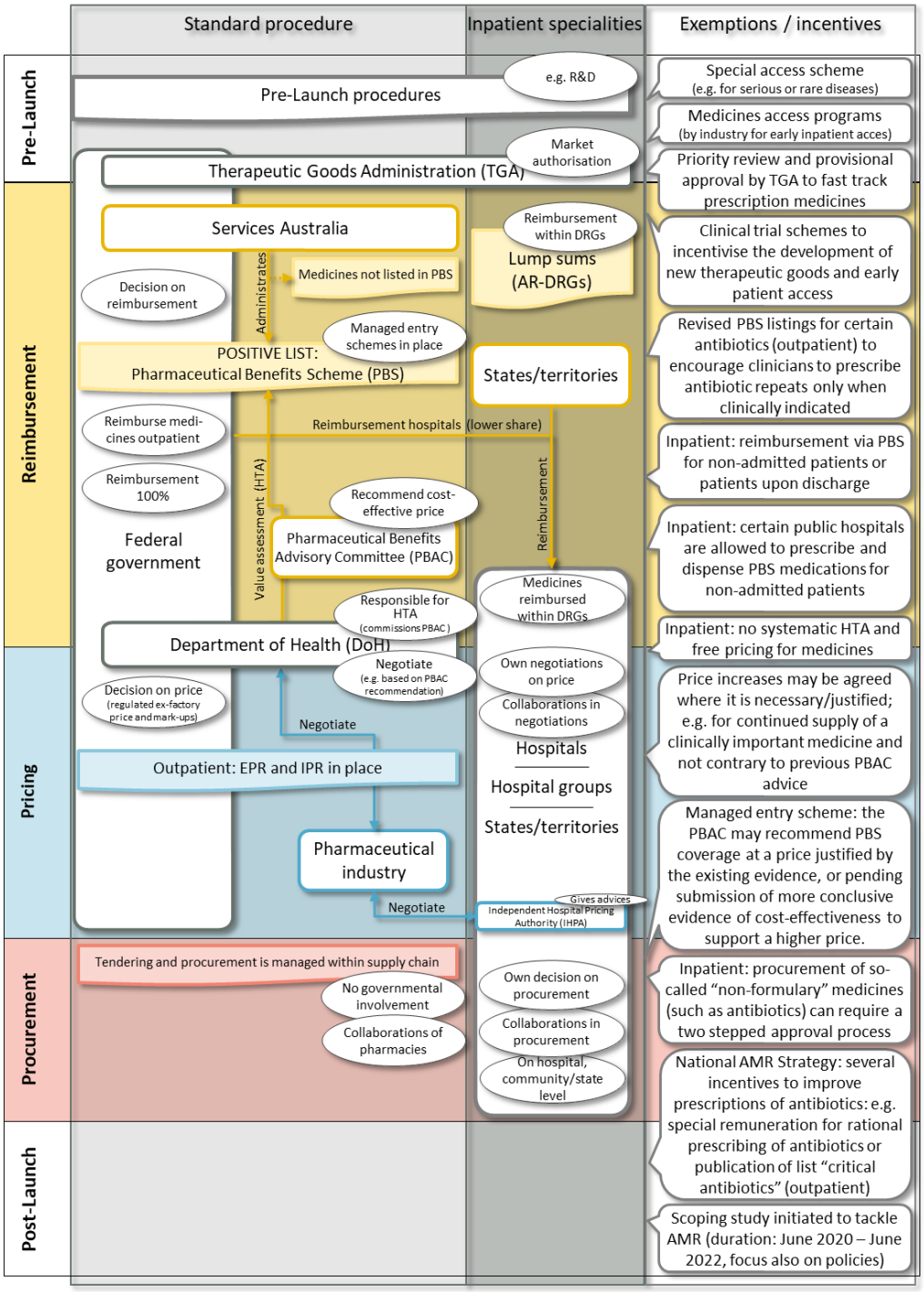
Context

Australia has a National Healthcare System (NHS), called Medicare, which is operated by Services Australia. It contains three major parts: medical services, public hospitals, and medicines. Medicare covers the cost (full or in parts) of: public hospital services, services provided by general practitioners and medical specialists, physiotherapy, community nurses and basic dental services for children [212].

An important part of Medicare is the Pharmaceutical Benefits Scheme (PBS). The PBS subsidises prescription medication and regulates prices and funding of medicines. The Medicare Benefits Schedule (MBS) is a list of all health services that the Government subsidises [213–215].

The Australian and state and territory governments broadly share responsibility for funding, operating, managing and regulating the health system. Whereas the federal government is responsible for the development of national health policies, funding of medical services through Medicare and medicines through the PBS and provision of funds to states and territories for public hospital services, the state and territory governments fund and manage public hospitals, regulate and license private hospitals and other health premises, regulate products with health impacts such as alcohol and tobacco, and deliver community-based and preventive services (for example, cancer screening and immunisation), or ambulance services [212, 216].

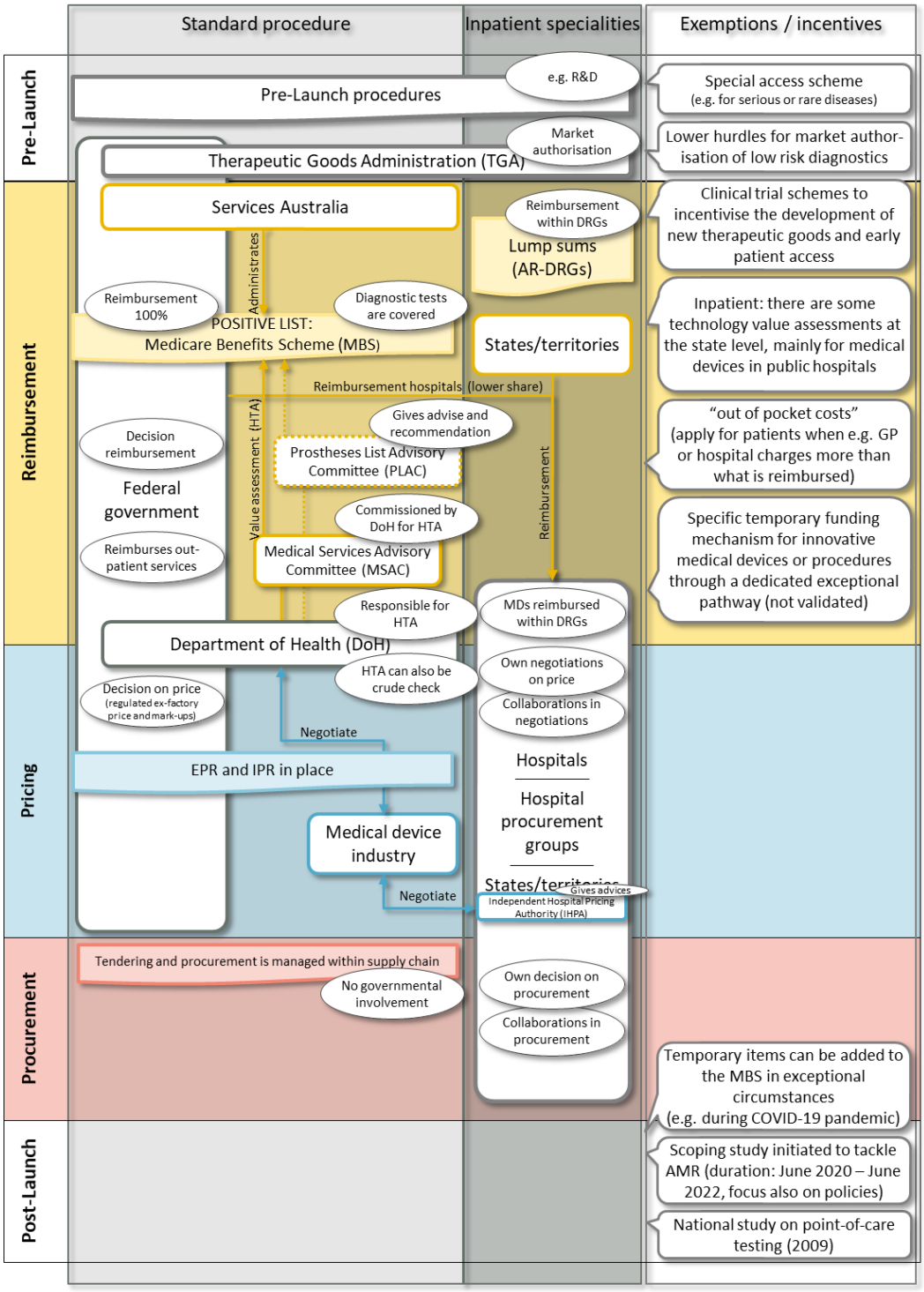
Pharmaceutical policy framework



AR-DRG = Australian Refined diagnosis-related groups; DRG = diagnosis-related groups; EPR = External Price Referencing; HTA = Health Technology Assessment; IPR = Internal Price Referencing; R&D = Research and Development

Source: GÖ FP survey

Policy framework for medical devices



AR-DRG = Australian Refined Diagnosis Related Groups, DRG = diagnosis-related groups; EPR = External Price Referencing, HTA = Health Technology Assessment, IPR = Internal Price Referencing, R&D = research and development

Source: GÖ FP survey

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7.2.2 Brazil

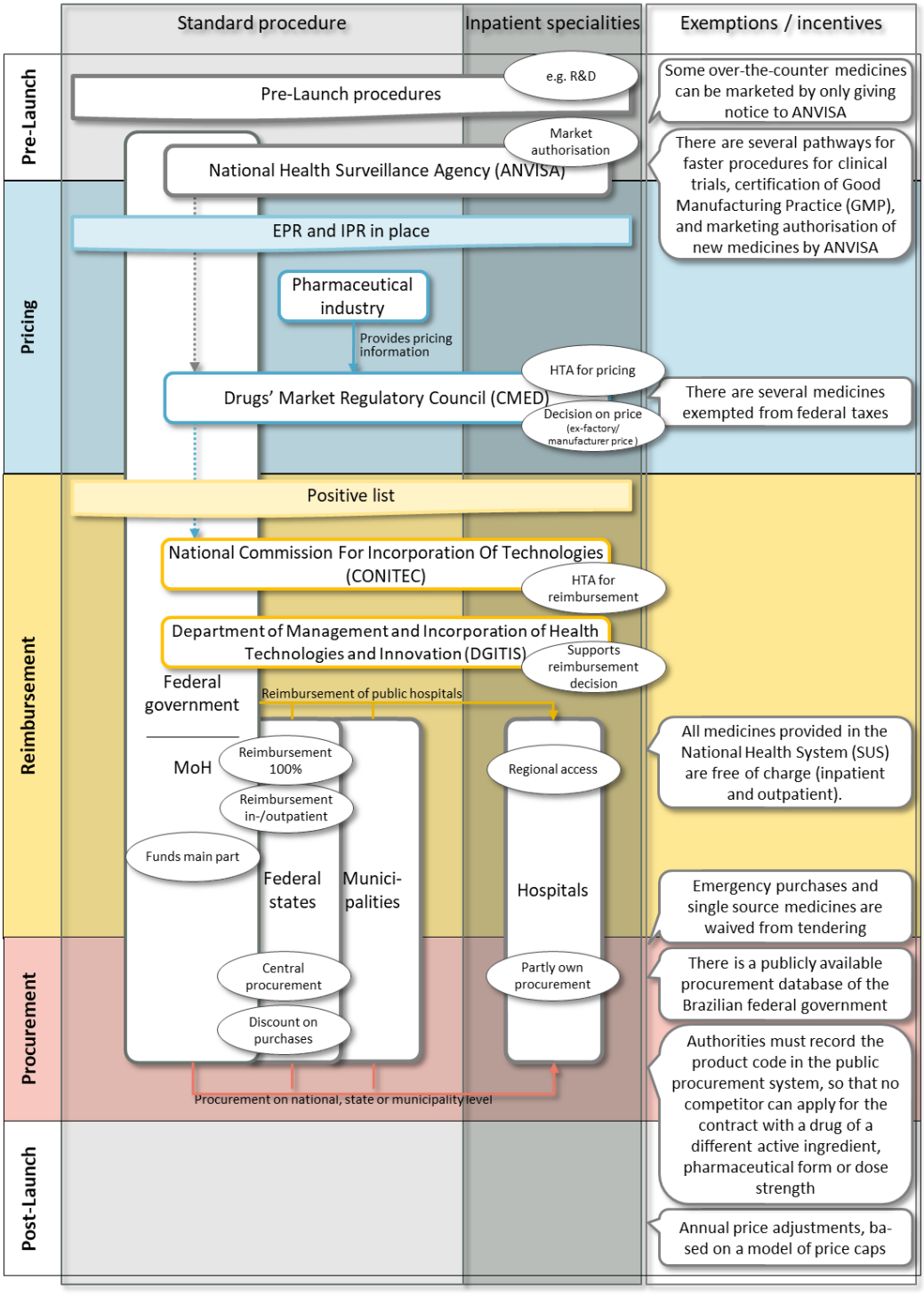
Context

Brazil has a National Healthcare System (NHS), known as the Unified Health System (Portuguese: Sistema Único de Saúde, SUS). The SUS is universal and free for everyone, ensuring universal access to health. SUS is financed with general taxes and social contributions collected by the three levels of government (federal, state and municipal). Primary healthcare remains the responsibility of the federal government, whereas elements (such as the operation of hospitals) are overseen by individual states [217].

Services under the public SUS system are available to all Brazilians without user fees, co-payments or financial contributions, except for medicines, where co-payments are necessary. The combination of out-of-pocket and private insurance spending is over 50% [218].

A characteristic of the Brazilian pharmaceutical system is that – after market approval – pricing procedures apply (including HTA for pricing), followed by reimbursement decisions (including HTA for reimbursement) [219, 220].

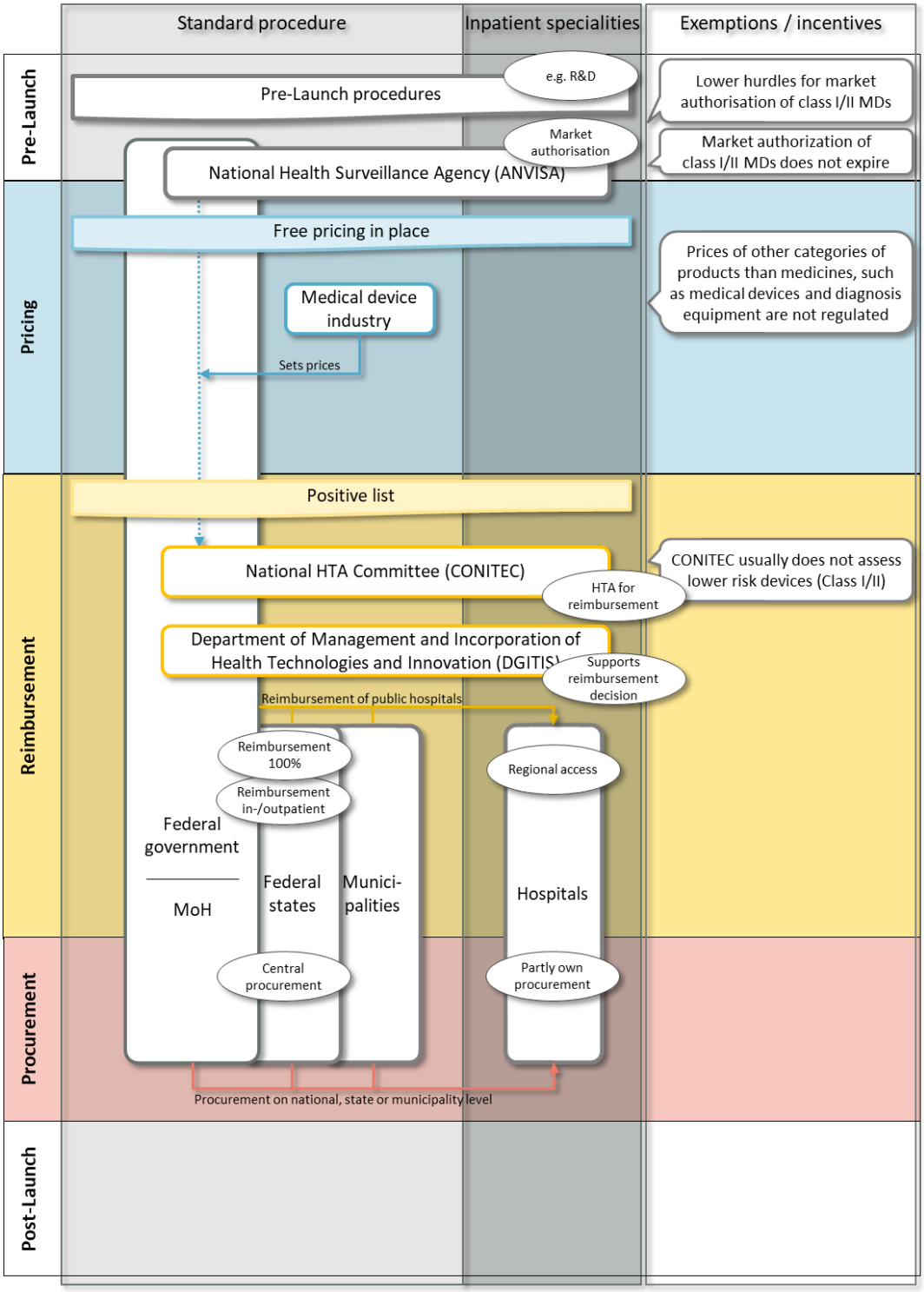
Pharmaceutical policy framework



EPR = External Price Referencing, HTA = Health Technology Assessment, IPR = Internal Price Referencing, MoH = Ministry of Health, R&D = research and development

Source: GÖ FP survey

Policy framework for medical devices



HTA = Health Technology Assessment, MoH = Ministry of Health, R&D = research and development

Source: GÖ FP survey

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7.2.3 France

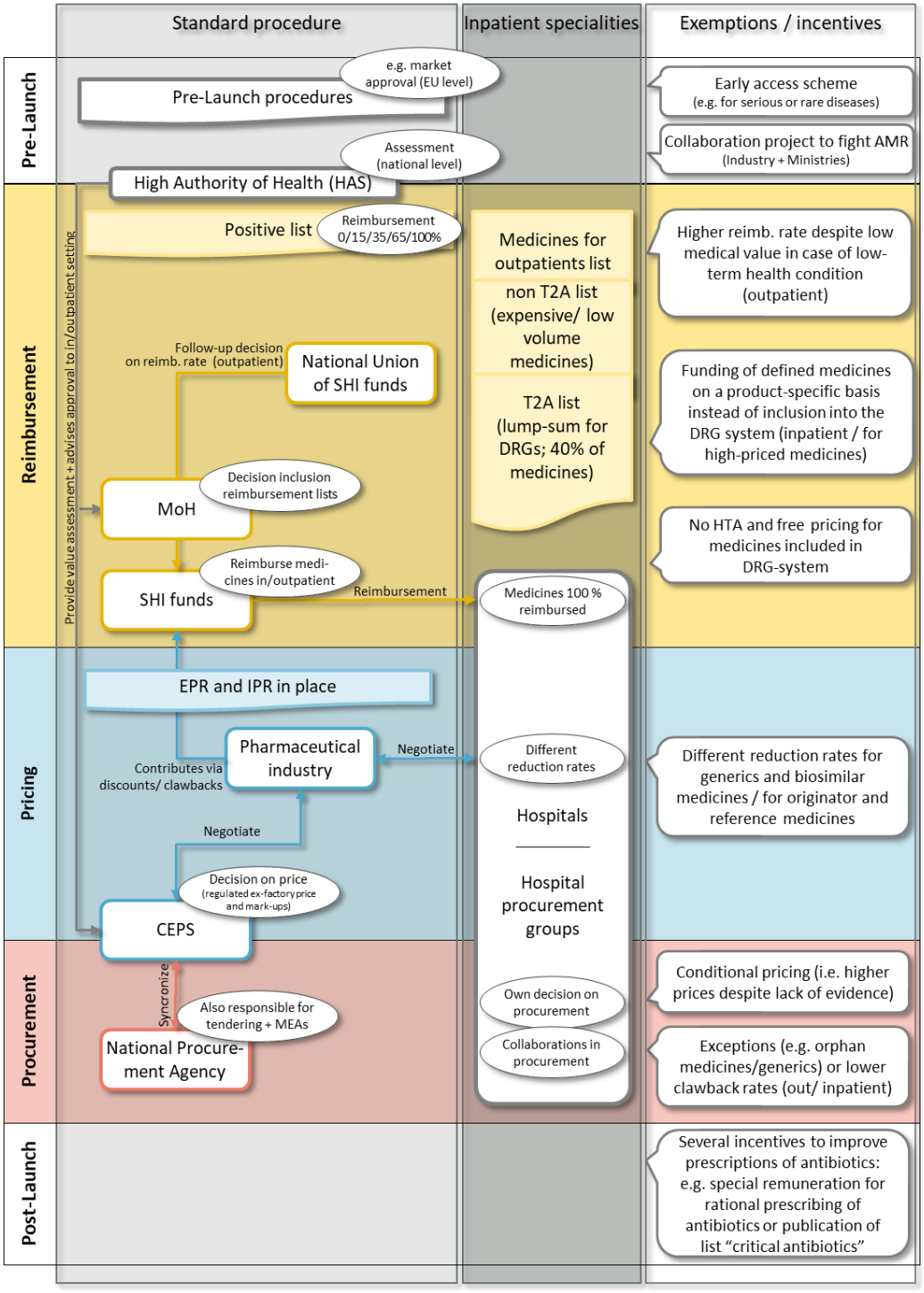
Context

The French health care and pharmaceutical system is based on the Bismarckian approach of a Social Health Insurance system, supplemented by complementary health insurances (so-called "mutuelles"). Thus, the Social Security Code (Code de la sécurité sociale / CSS) is a major legal basis of the pharmaceutical policy framework, adding to relevant provisions in the Public Health Code (Code de la santé publique / CSP). In addition, the French government and the health insurance institutions, represented by the Economic Committee for Health Care Products (Comité économique des produits de santé, CEPS) and the pharmaceutical industry association (Les Entreprises du medicament / LEEM) have concluded multi-annual framework agreements (Accords Cadre) which defined specificities of the price negotiation procedure.

The competences for regulatory and pharmaceutical policy matters (such as marketing authorisation, pricing and reimbursement) are divided among public authorities. In principle, the same public institutions are responsible for policy implementation in the outpatient and inpatient sectors, however, processes differ. Linkage exists between pricing and reimbursement policies.

Key competent authorities for pricing and reimbursement in France are the Ministry of Solidarity and Health (Ministère des Solidarités et de la Santé) and the Ministry of Economy and Finance (Ministère de l'Économie et des Finances). The Economic Committee for Health Care Products, CEPS, affiliated to the Ministry of Solidarity and Health is in charge of pricing medicines. The decision on the reimbursement level per medicine is taken by the National Union of Health Insurance Funds (Union nationale des caisses d'assurance maladie, UNCAM), and the sickness funds (health insurances) and the "mutuelles" offer reimbursement. The Social Health Insurance is also in charge of funding medicines in the inpatient sector. CEPS and UNCAM take their decisions based on health technology assessments (HTA) provided by the Transparency Commission of the High Authority of Health (Haute Autorité de Santé / HAS). The Transparency Commission of HAS also advices the Ministry of Solidarity and Health if a medicine should be approved for use in the outpatient sector, in the inpatient sector or both. The French Medicines Agency (Agence nationale de sécurité du médicament et des produits de santé / ANSM) is not involved in pricing and reimbursement matters but it is in charge of marketing authorisation, pharmacovigilance and inspections and also early access authorisation.

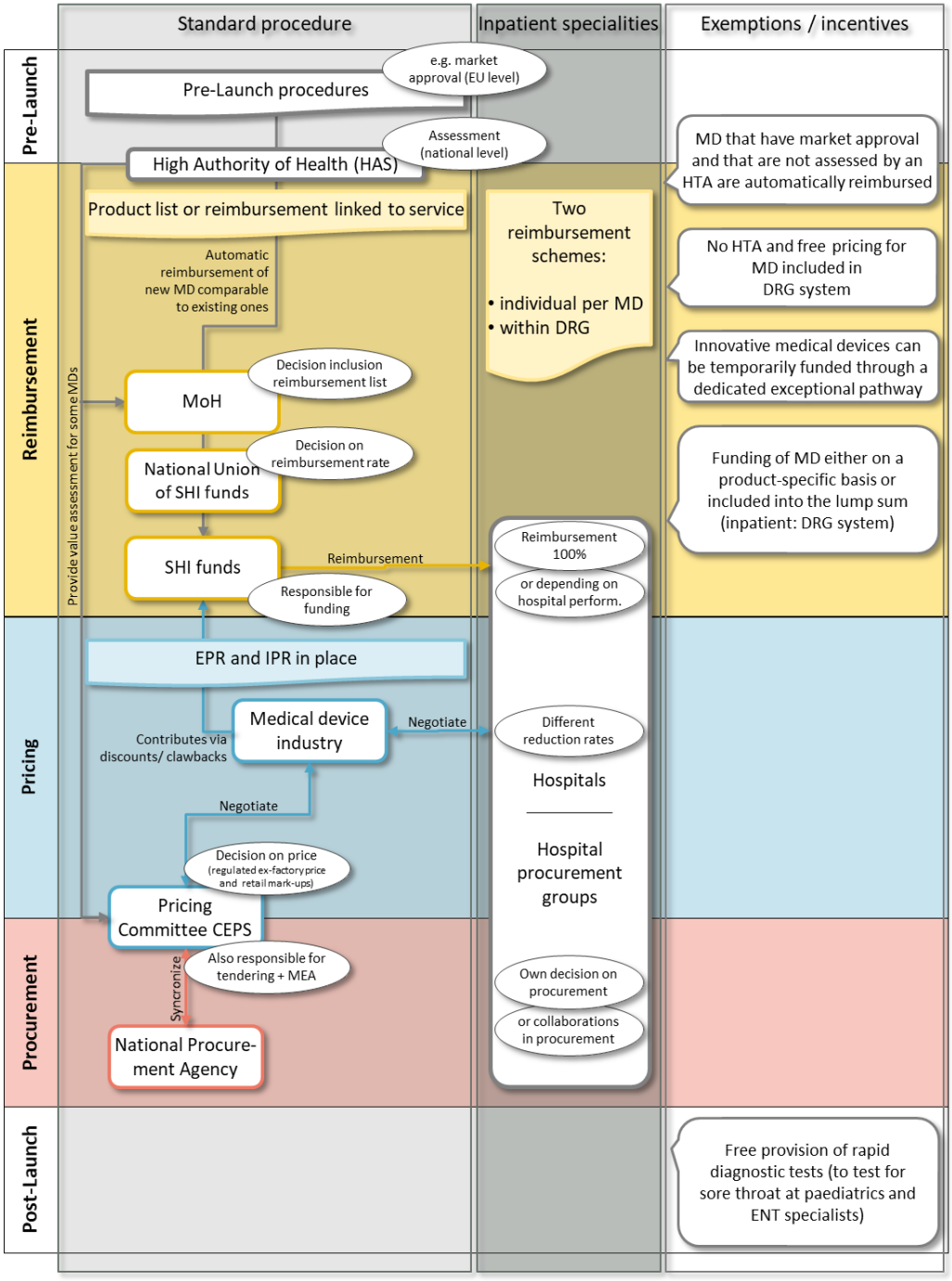
Policy framework for medicines



CEPS = Comité économique des produits de santé / Economic Committee for Health Care Products, EPR = External Price Referencing, IPR = Internal Price Referencing, MoH = Ministry of Health, SHI = social health insurance

Source: GÖ FP survey

Policy framework for medical devices



ENT = ear, nose and throat, CEPS =Comité économique des produits de santé / Economic Committee for Health Care Products, EPR = External Price Referencing, IPR = Internal Price Referencing, MoH = Ministry of Health, SHI = social health insurance

Source: GÖ FP survey

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7.2.4 Germany

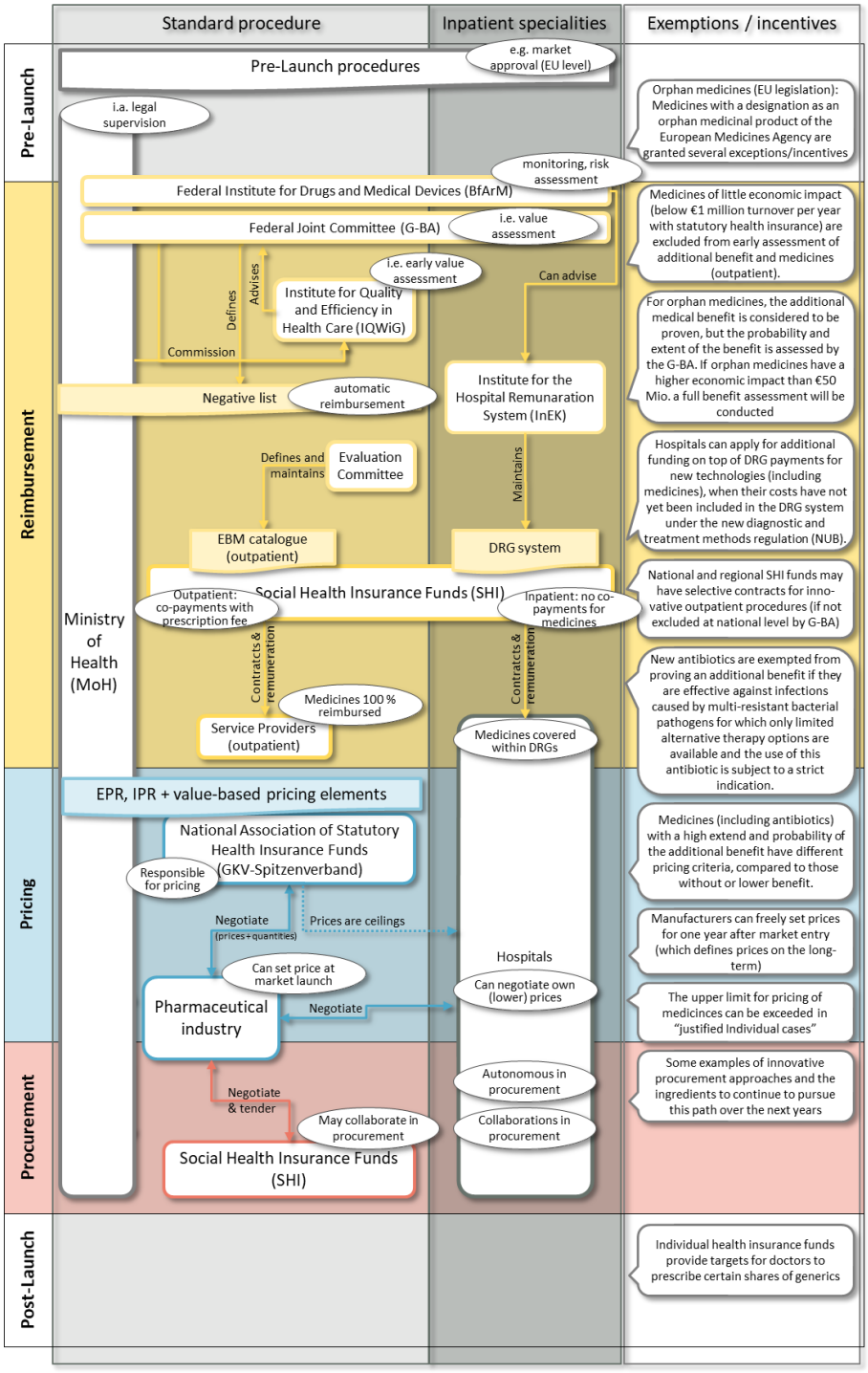
Context

Germany has a universal multi-payer health care system paid for by a combination of statutory health insurance (Gesetzliche Krankenversicherung) and private health insurance (Private Krankenversicherung) [221].

Since 2009, health insurance has been compulsory for the whole population in Germany, when coverage was expanded from the majority of the population to everyone. Workers and employees with a salary below a certain threshold (as of 2020: €62,550 per year or €5,212.50 per month) are automatically enrolled into one of the non-profit sickness funds. Insurance contributions are co-financed by employer and employee and includes, beside health insurance, accident insurance, and long-term care insurance [221].

Pharmaceutical pricing and reimbursement policies are based on the following principles: prescription drugs are reimbursed by the health insurance unless included in a negative list; manufacturers are free to set their price; drugs can be clustered in groups of products considered to be therapeutically equivalent and subject to maximum reimbursement amounts [221].

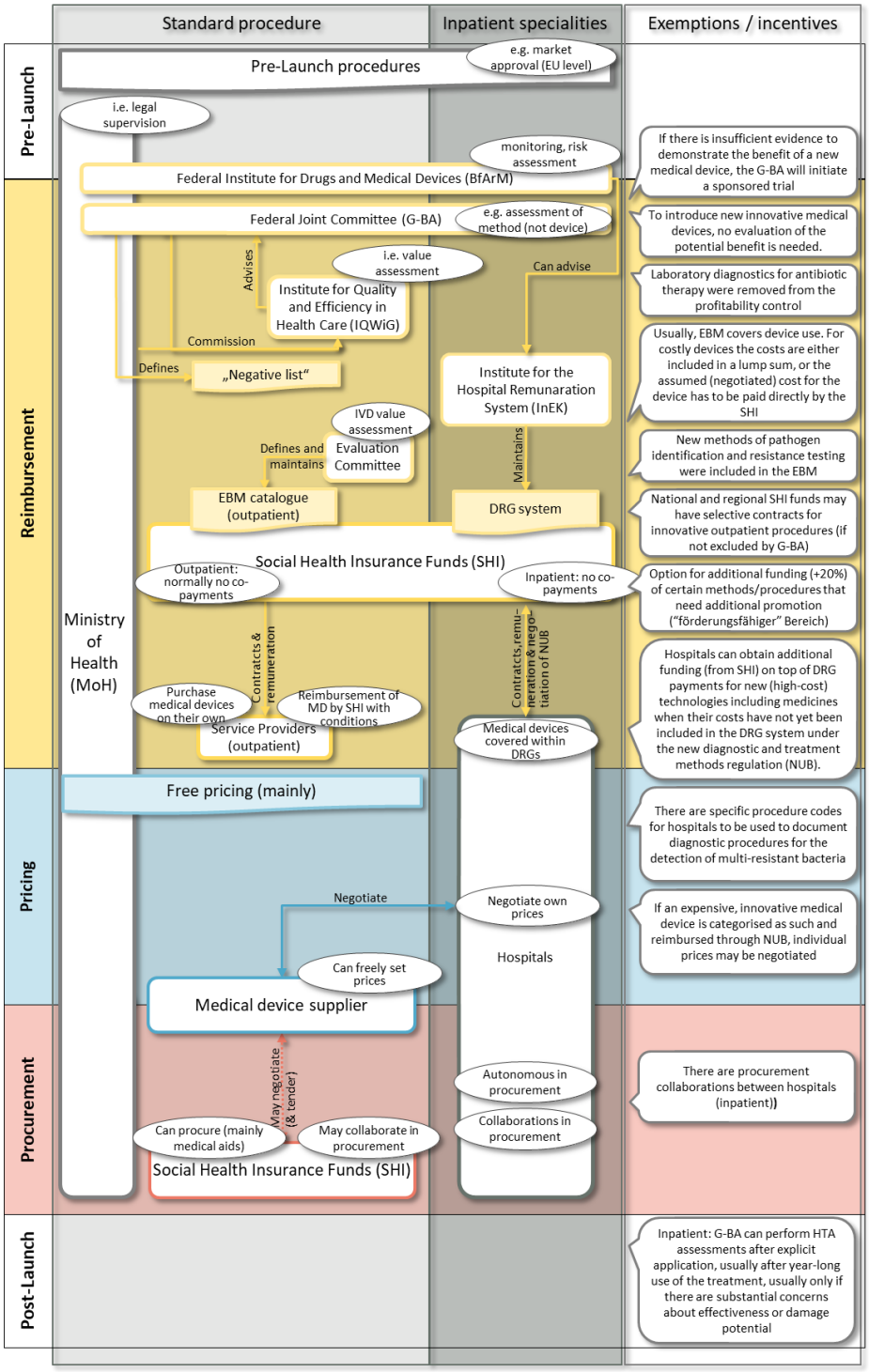
Pharmaceutical policy framework



DRG = diagnosis-related groups, EBM = evidence-based medicine, EPR = External Price Referencing, HTA = Health Technology Assessment, IPR = Internal Price Referencing, MoH = Ministry of Health, SHI = social health insurance

Source: GÖ FP survey

Policy framework for medical devices



DRG = diagnosis-related groups, IVD = in vitro diagnostic, MoH = Ministry of Health, SHI = social health insurance

Source: GÖ FP survey

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7.2.5 Italy

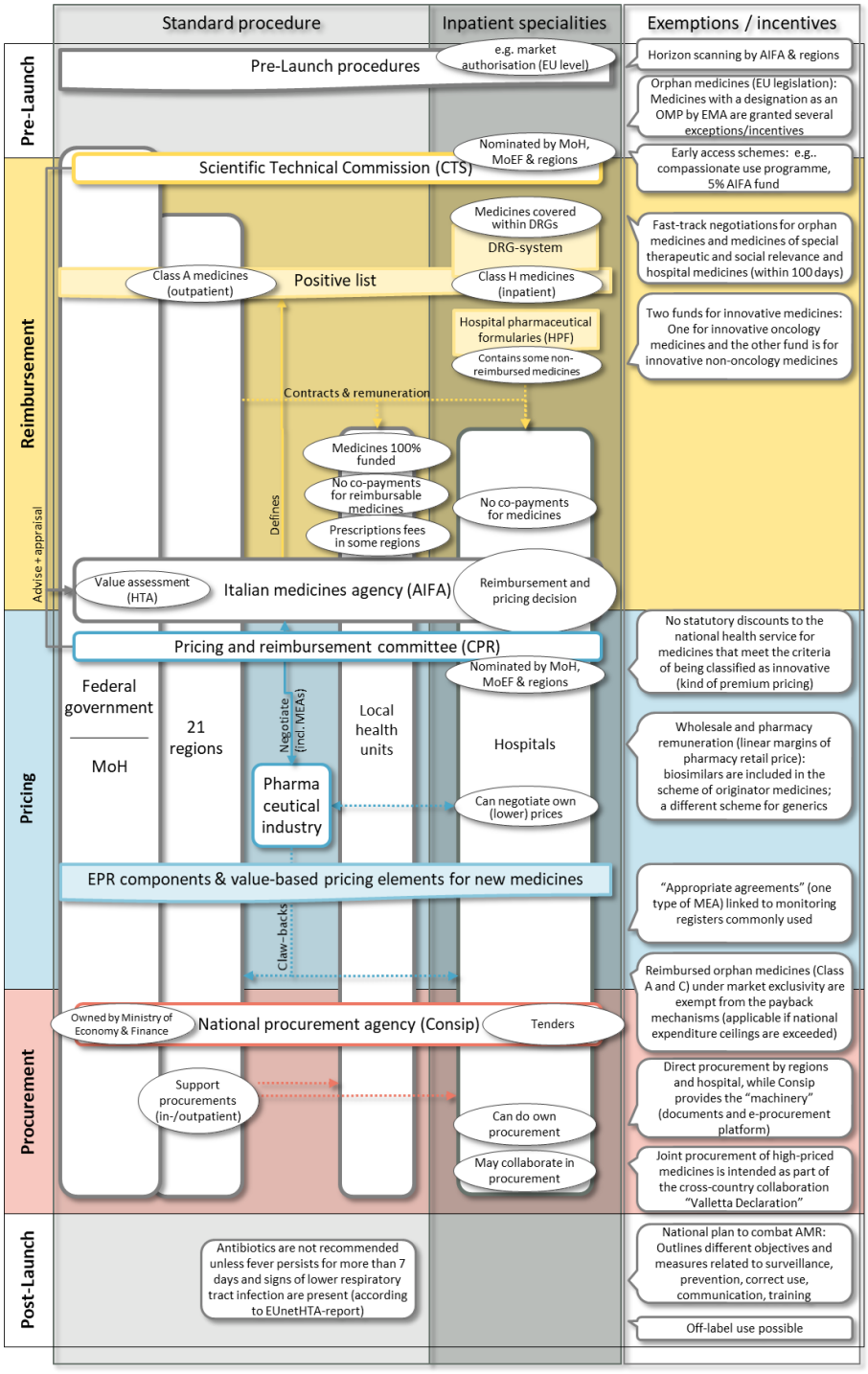
Context

Health and pharmaceutical care in Italy is based on the National Health Service (called Servizio Sanitario Nazionale / SSN). The SSN is organised into three tiers: the central government, 21 regions and the local health units (local health authorities (Aziende Sanitarie Locali / ASL) and public so-called "Independent Hospitals" (Aziende Ospedaliere /AO). Health care is a matter of shared jurisdiction between the central government and the regions, and in the regions, the respective ASL are responsible for the health of the entire population in their area.

The Italian SSN is mainly financed by national and regional taxes; some patient co-payments also apply. The central government defines the economic and financial programme with a proposal for the next year's national budget and for the next three calendar years, which is outlined in the annual Budget Law ("Legge Finanziaria"), which also establishes the amount to be spent by the Government on health care ("spending ceilings"). Funds assigned to the regions are intended to cover the provision of the so-called Essential Care Levels which define a minimum of health care services provided by the governments. In the pharmaceutical sector, regions are the key funders for medicines.

The key public institution in the pharmaceutical sector is the Italian Medicines Agency (Agenzia Italiana del Farmaco, AIFA). It is responsible for all matters regarding the medicines for human use, including market authorisation, pharmacovigilance, and pricing and reimbursement.

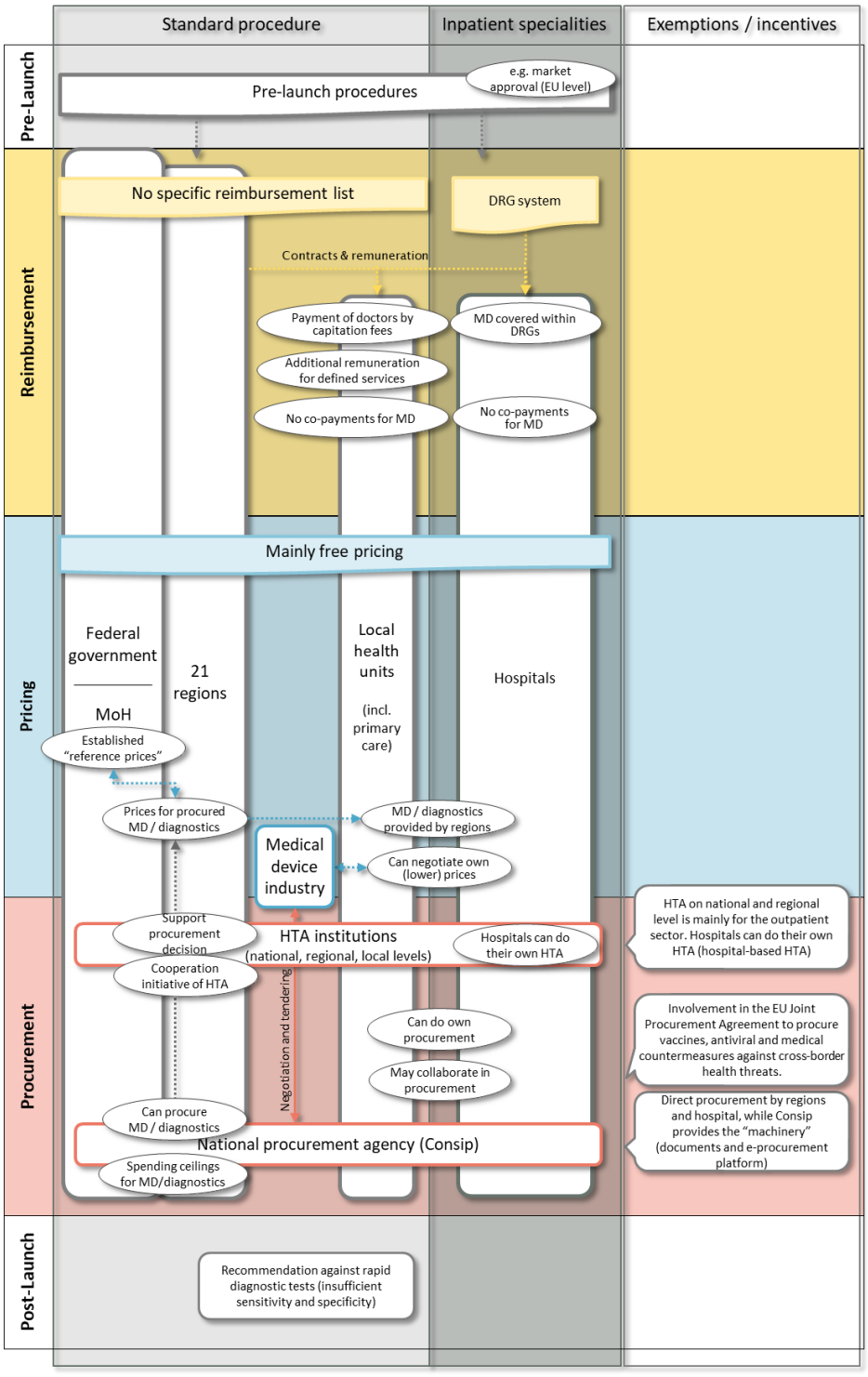
Policy framework for medicines



DRG = diagnosis-related groups, EPR = External Price Referencing, HTA = Health Technology Assessment, MoEF = Minstry of Economy and Finance, MoH = Ministry of Health

Source: GÖ FP survey

Policy framework for medical devices



DRG = diagnosis-related groups, HTA = Health Technology Assessment, MoH = Ministry of Health

Source: GÖ FP survey

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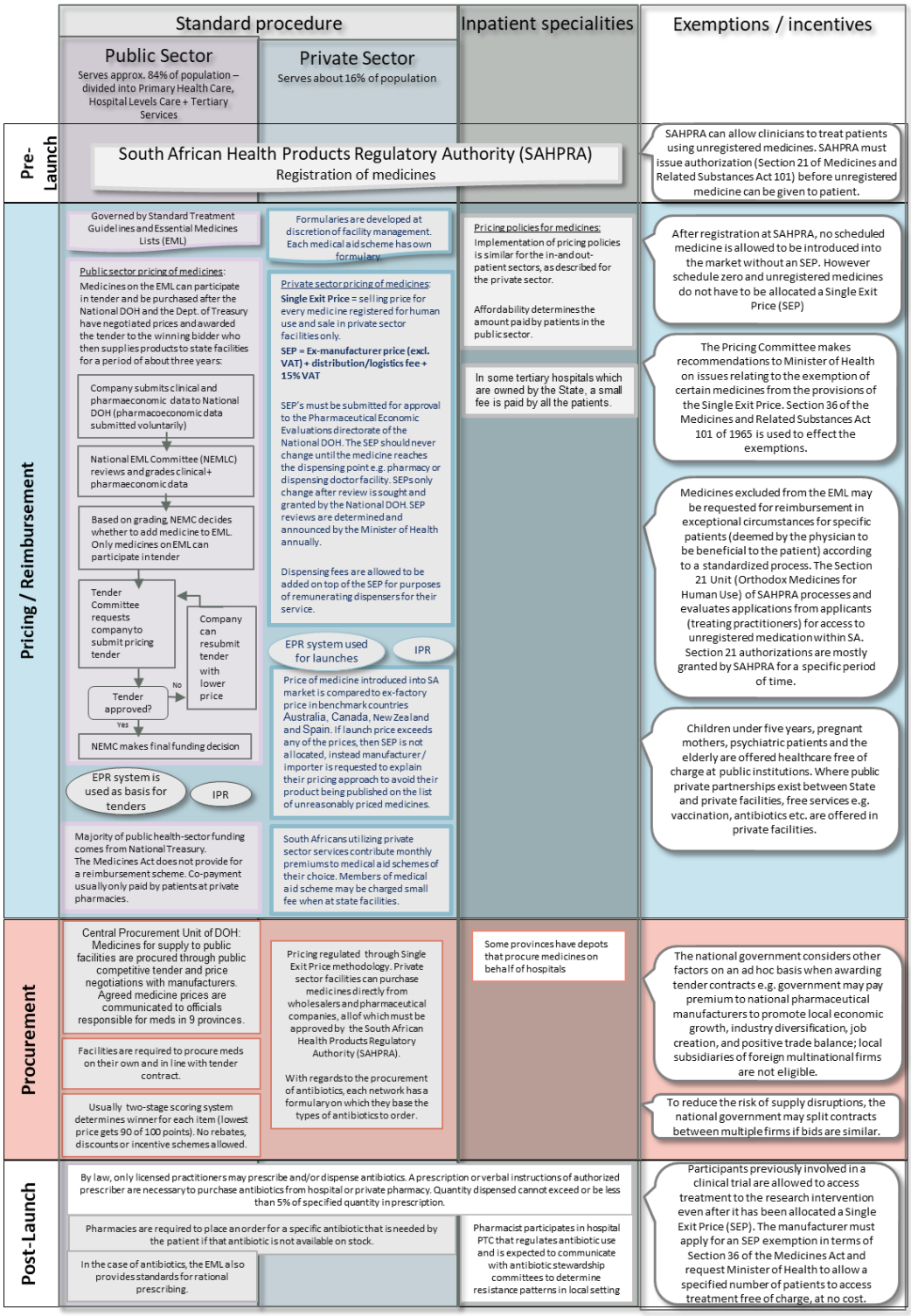
7.2.6 South Africa

Context

South Africa has a two-tiered healthcare system, comprising both the public and private sectors. The public sector is managed by the government, providing health care services to around 84% of the population (48 million people). The private sector serves approximately 16% of the population, yet accounts for 84% of total pharmaceutical expenditure in the country. Healthcare services delivered in the public sector are predominantly funded through general tax revenues allocated to health budgets. In the private sector, which caters to patients with private medical insurance, healthcare services are largely financed via medical aid schemes with a small proportion financed via out-of-pocket payments.

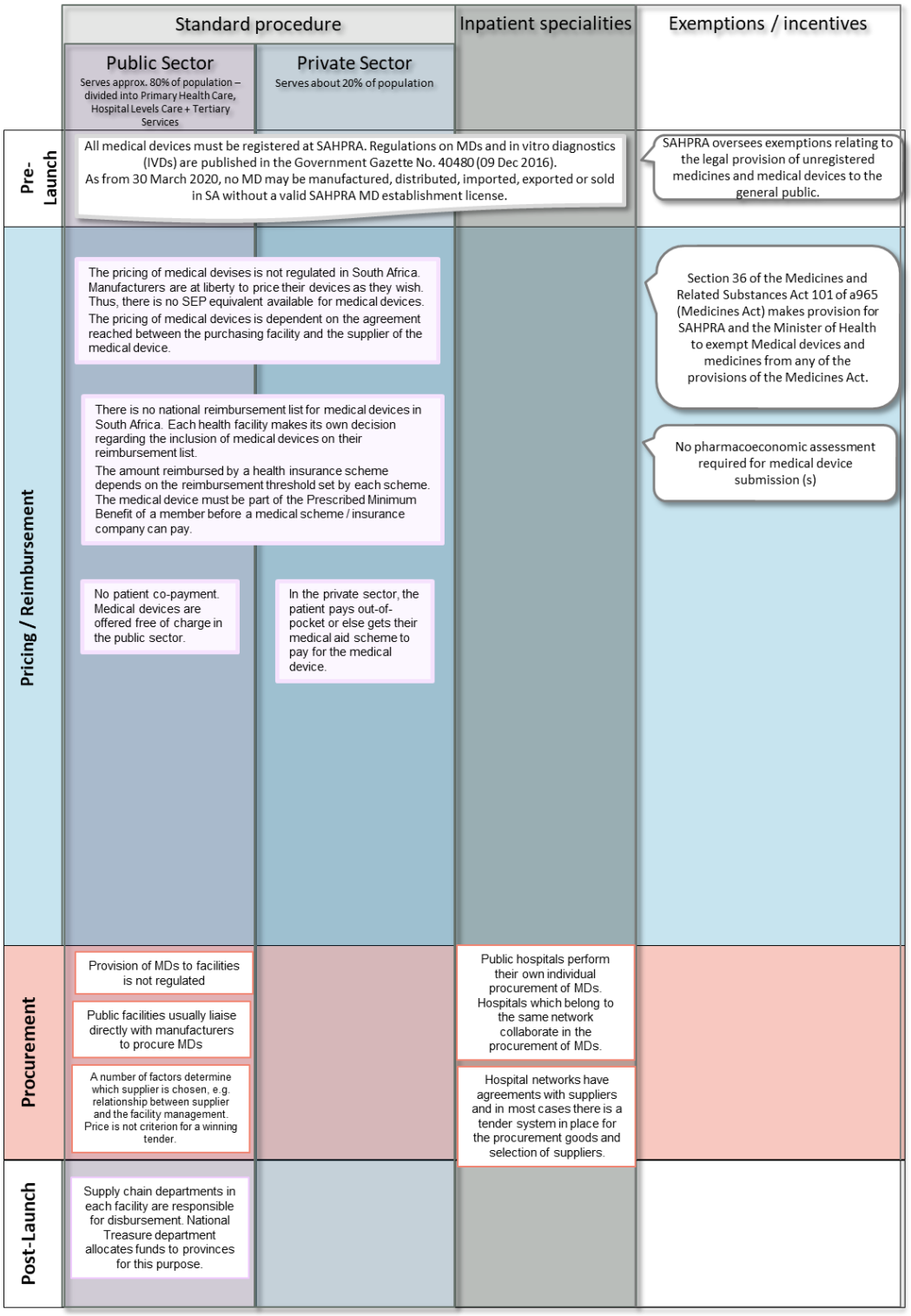
The key regulatory authority for medicines, established by the Medicines Act, is the South African Health Products Regulatory Authority (SAHPRA). SAHPRA's responsibilities include the registration of medicines for sale and ensuring the safety and efficacy of medicines manufactured, imported and sold in South Africa. Since 2016, the regulation of medical devices has been included under the Medicines Act. For the public sector, the National Department of Health procures medicines on the Essential Medicines List from manufacturers through a public tender system. In the private sector, prices of all medicines sold in South Africa are regulated by the "single exit price" policy, which prohibits discounts and rebates and aims to ensure price transparency in the sector. The Medicines Act and its regulations do not provide for a reimbursement scheme; the national healthcare policy is funded out of the Department of Health's budget, to which the Department of Health and the Treasury agreed.

Pharmaceutical policy framework



Source: GÖ FP survey

Policy framework for medical devices



Source: GÖ FP survey

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7.2.7 Saudi Arabia

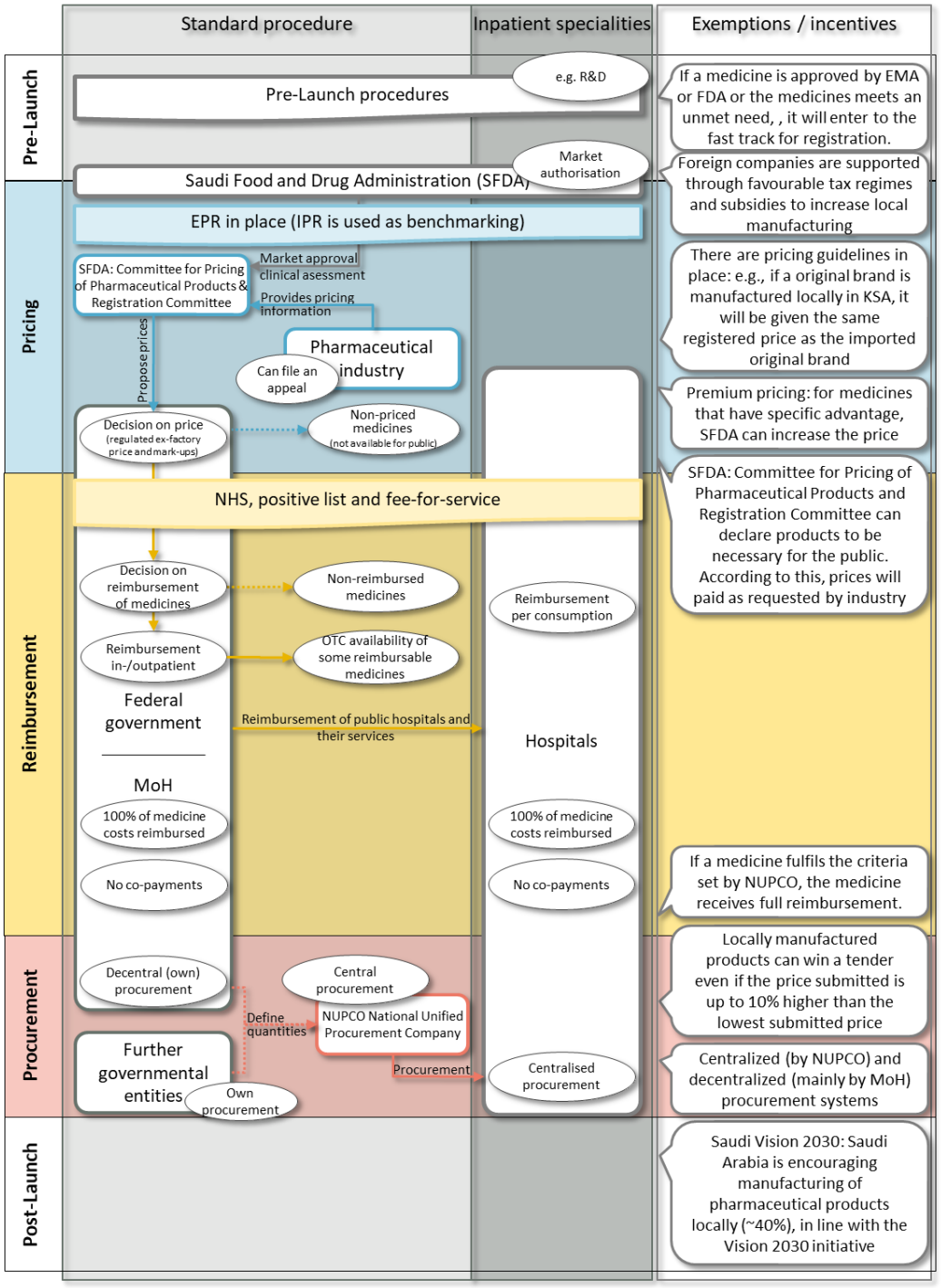
Context

Currently, the Ministry of Health is the major provider and funder for all levels of health care services in Saudi Arabia. These services comprise 60 % of the total health services in Saudi Arabia. The other government bodies include, for instance, referral hospitals, security forces medical services, army medical services, National Guard health affairs, or Ministry of Higher Education hospitals [222].

In accordance with the Saudi constitution, the government provides all citizens and expatriates working within the public sector with full and free access to all public health care services – including pharmaceuticals [222].

Even though, to date the Saudi health care system is an Beveridge Model (thus, an NHS), there are intentions to slowly switch to a Bismarck Model, offering salary and insurance based health care.

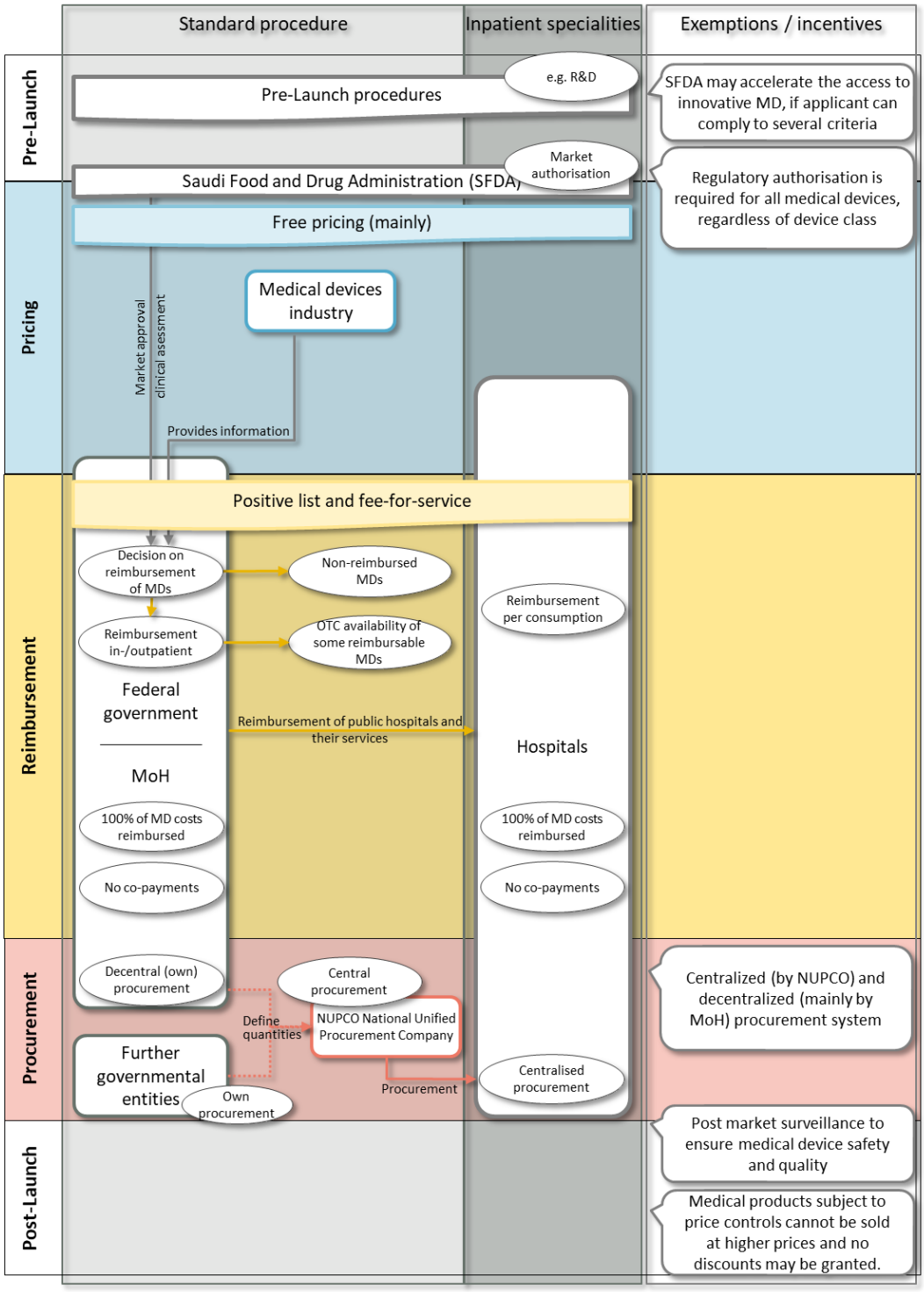
Pharmaceutical policy framework



EMA = European Medicines Agency , EPR = External Price Referencing, FDA = Food and Drug Administration, HTA = Health Technology Assessment; IPR = Internal Price Referencing, MoH = Ministry of Health; OTC = Over-the-Counter = non-prescription medicine; R&D = research and development

Source: GÖ FP survey

Policy framework for medical devices



MD = Medical Device; MoH = Ministry of Health

Source: GÖ FP survey

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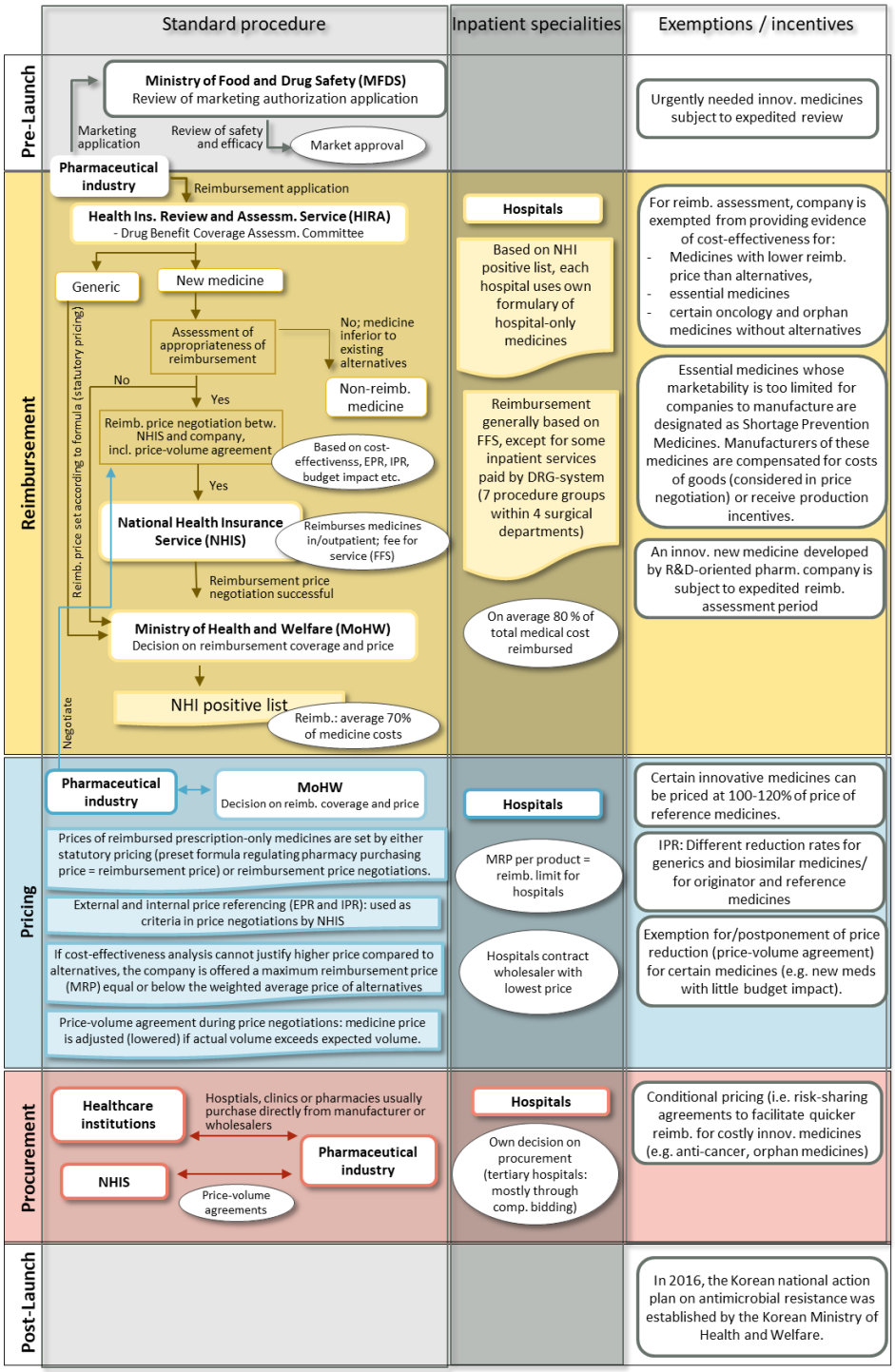
7.2.8 South Korea

Health and pharmaceutical care in South Korea is based on a social health insurance system, which provides universal health coverage to the population. The National Health Insurance Program is managed by the National Health Insurance Service (NHIS) and covers approximately 97% of the population. The remaining 3% are covered by the Medical Aid Program, which is a public assistance programme providing healthcare benefits to low-income families. The National Health Insurance Program and Medical Aid Program covers inpatient, outpatient, emergency services, dental and pharmacy services. Despite the universal healthcare safety net, a considerable portion of healthcare in South Korea is privately funded.

With public health care institutions providing only a small range of services, the majority of health care services are provided by private health care institutions. All medical institutions and pharmacies are required to provide services covered by the NHIS. The insurance system is financed by compulsory contributions from all residents, government subsidies, and tobacco surcharges. Although the NHIS is separate from the Ministry of Health and Welfare (MoHW), which is responsible for health policy and planning, and has control over national hospitals, the NHIS remains under some indirect control of the MoHW.

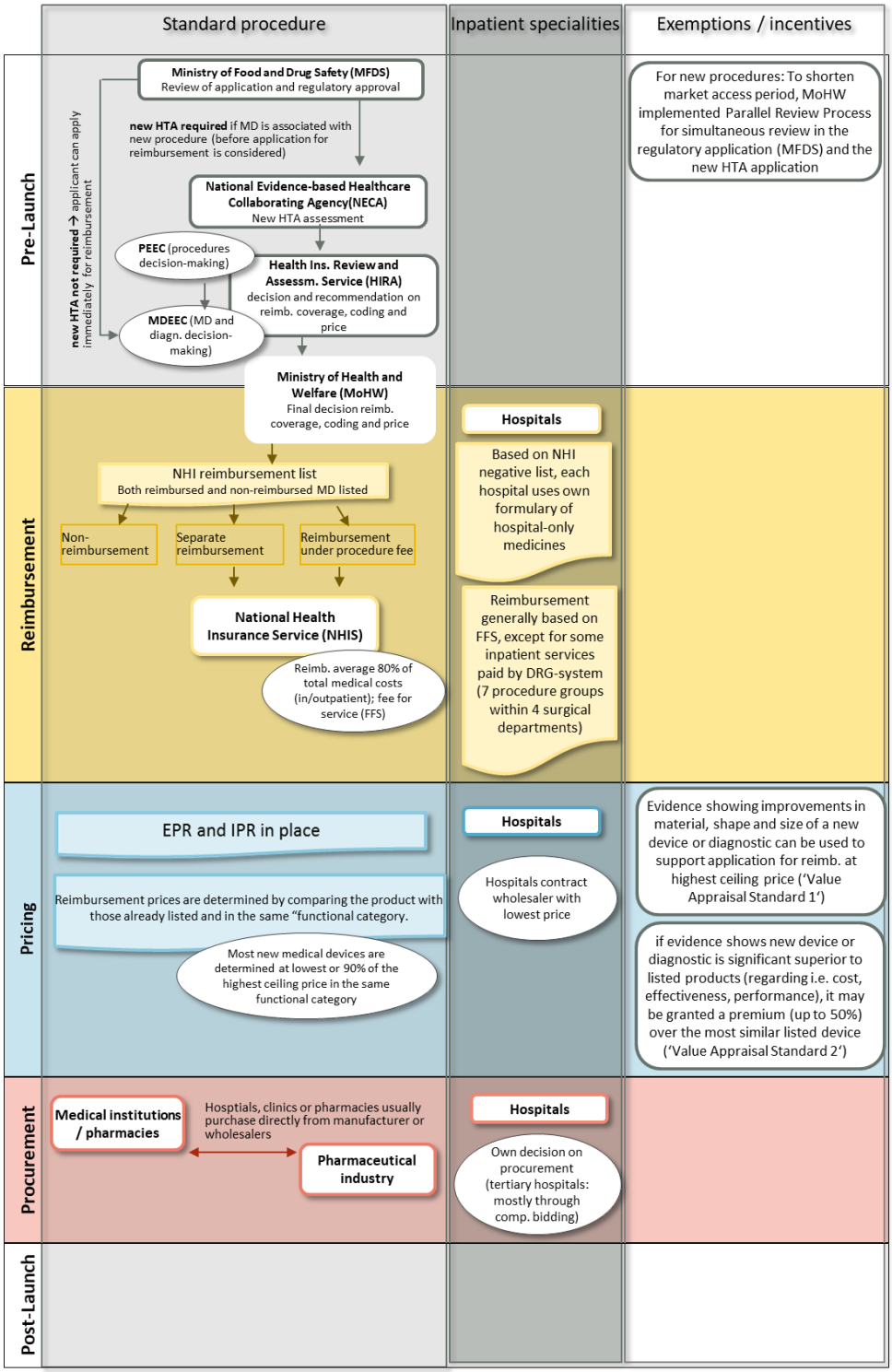
Further government organisations at the national level supporting the health care system include the Ministry of Food and Drug Safety (MFDS), and the Korea Centers for Disease Control and Prevention (KCDC). While the MFDS is in charge of the approval of foods, medicines, and medical devices, the KCDC is tasked with surveillance of infectious diseases nationally and internationally to prevent a national crisis. At the sub-national level, the regional governments supervise the regional medical centres and other medical facilities according to local needs.

Pharmaceutical policy framework



Source: GÖ FP survey

Framework for medical devices



Source: GÖ FP survey

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7.2.9 Spain

Context

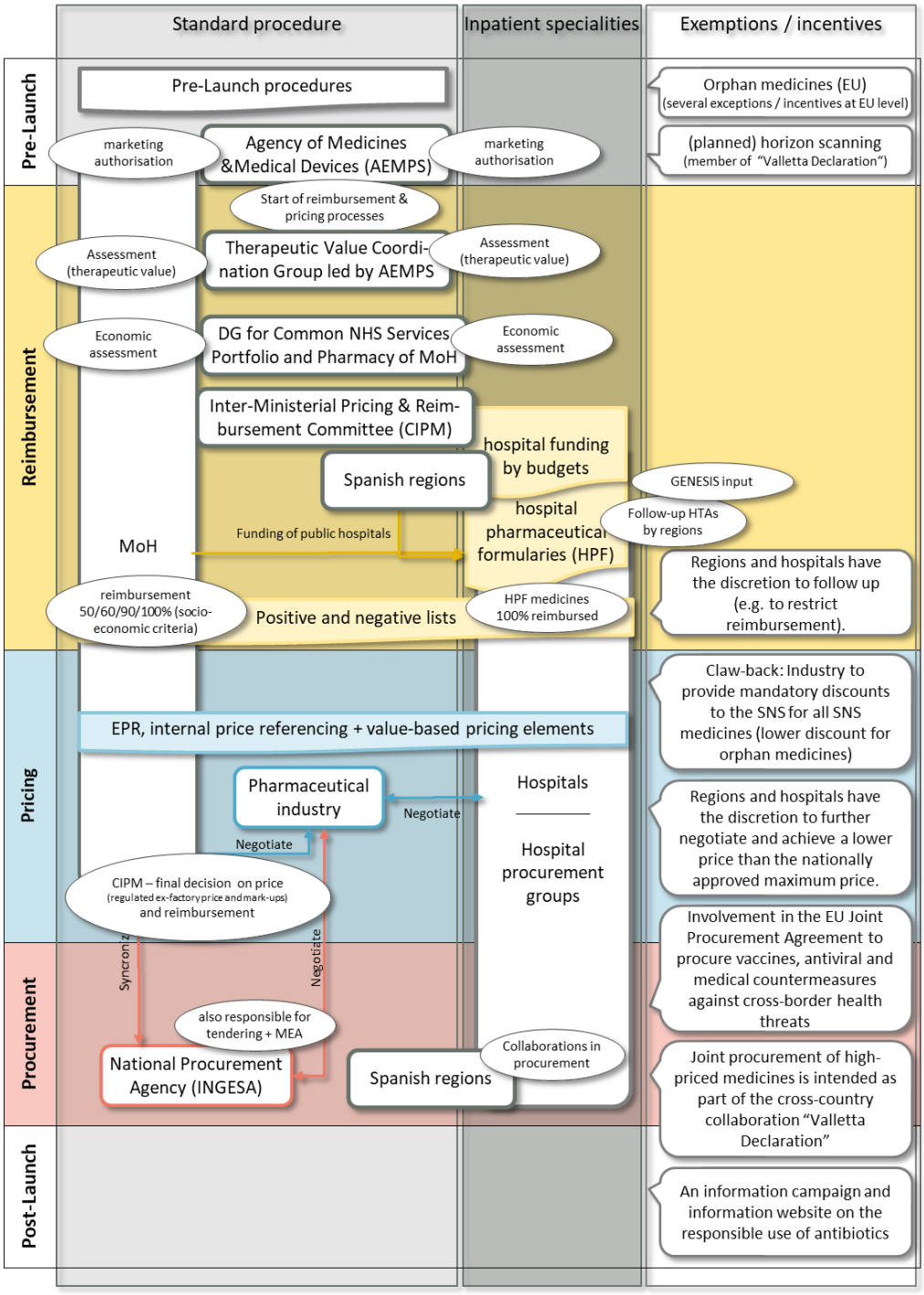
Health care in Spain is organised based on a National Health Service (NHS; Sistema Nacional de Salud / SNS), and each of the 17 Autonomous Regions has its own health service.

The Spanish Constitution of 1978 established the right to health care for all citizens. The key legal document for medicines is the Royal Decree 29/2006 on guarantees and rational use of medicines and health products (as amended by Royal Legislative Decree 1/2015 of 24 July). It is a comprehensive Medicines Act that regulates several aspects, including clinical research, marketing authorisation, prescription and dispensing, procedure for public funding and rational use of medicines. In 2012, during the global financial crisis, Royal Decree 16/2012, on urgent measures for the sustainability of the SNS, introduced cost-containment measures in the pharmaceutical sector .

As of 2020, key authorities at federal level are the Agency of Medicines and Medical Devices (Agencia Española de Medicamentos y Productos Sanitarios / AEMPS), which is responsible for marketing authorisation and also for clinical assessments of medicines and the Ministry of Health (Ministerio de Sanidad). The relevant unit of the MoH, which performs Health Technology Assessments (HTA) and prepares pricing and reimbursement decisions on medicines, is the Directorate General for Common NHS Services Portfolio and Pharmacy (DG de Cartera Común de Servicios del SNS y Farmacia). Final decisions on pricing and reimbursement of medicines are taken by the Inter-Ministerial Pricing and Reimbursement Committee (Comisión Interministerial de Precios de los Medicamentos / CIPM) assigned to the MoH. The CIPM has representation of the MoH, other Federal Ministries (Ministry of Finance and Civil Service Ministry Industry, Trade and Tourism, Ministry of Economy and Competitiveness, and health representatives of all Regional Governments). CIPM decisions are applicable to all medicines used in the Spanish SNS (outpatient and inpatient sectors). Regions have some discretion to conduct some follow-up action on the pricing and reimbursement decision.

There are several HTA institutions at regional levels (e.g. Escuela Andaluza de Salud Pública, Agencia d'Avaluació de Tecnologies Sanitàries, Agencia de Evaluación de Tecnologías Sanitarias) which perform HTA on a broad range of health technologies including medicines. Their HTA reports are taken into consideration in pharmaceutical pricing and reimbursement decisions.

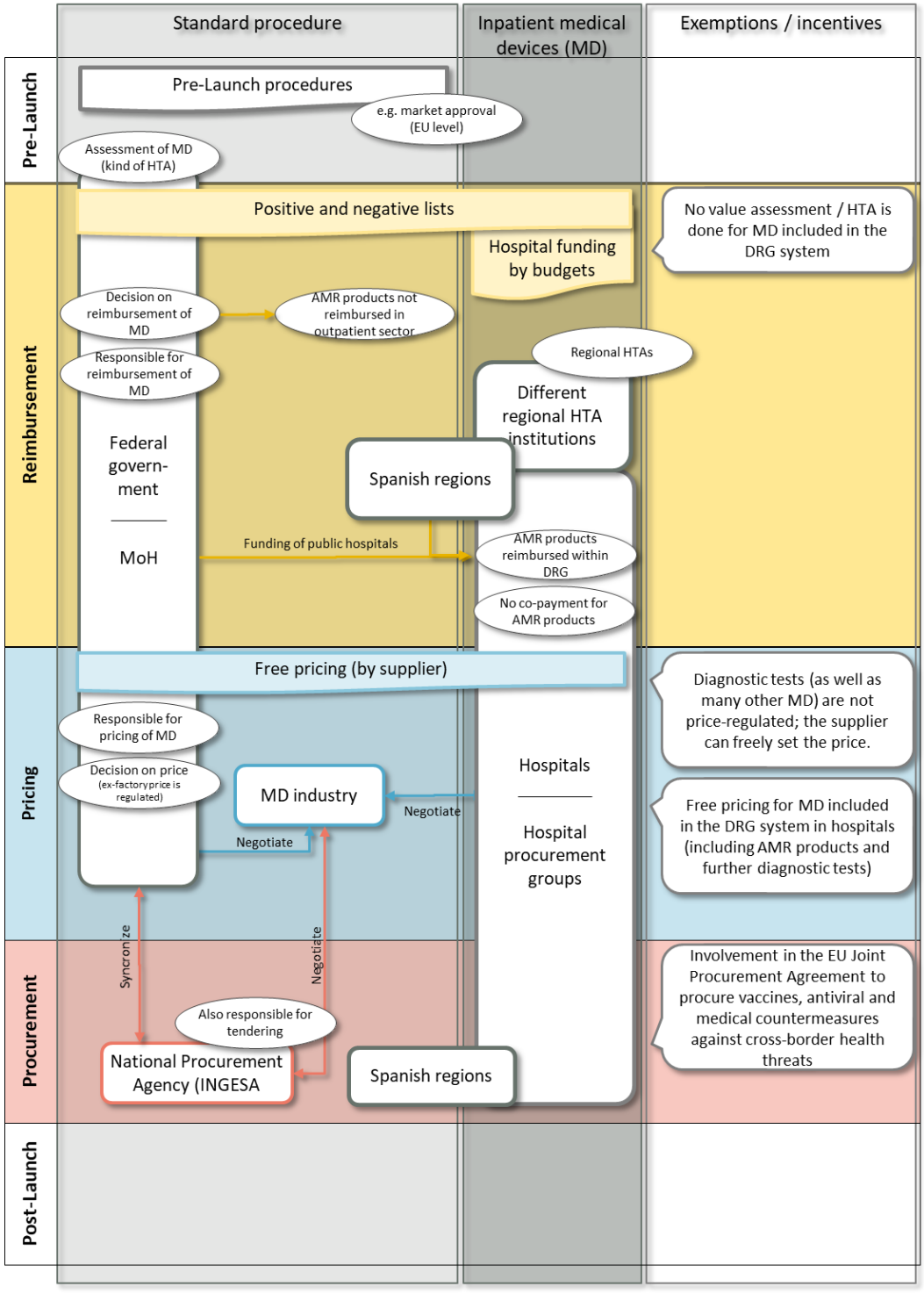
Policy framework for medicines



DG = Directorate General, EPR = External Price Referencing, HTA = Health Technology Assessment, MoH = Ministry of Health, NHS = National Health Sevice

Source: GÖ FP survey

Policy framework for medical devices



DRG = diagnosis-related groups, HTA = Health Technology Assessment, MoH = Ministry of Health

Source: GÖ FP survey

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7.2.10 Turkey

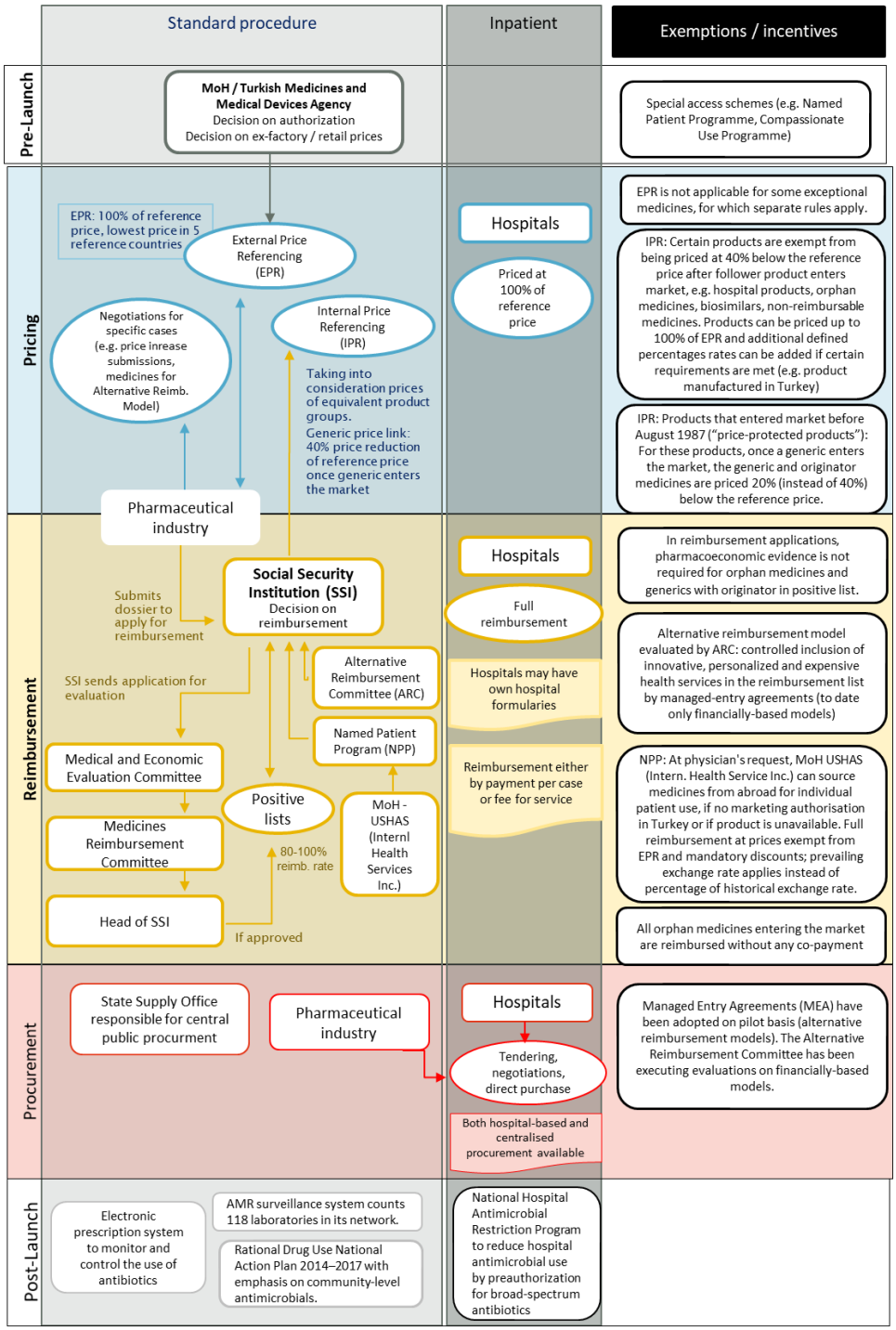
Context

Turkey's healthcare system underwent a full reform under the 2003-2013 Health Transformation Program, which saw the implementation of drastic changes in the provision and the financing of health care services leading to a rapid increase in health insurance coverage, range and quality of health services across the country.

Health services are now financed through a social security scheme covering more than 98% of the population, with the Social Security Institution (SSI) being the single purchaser for health services provided by both public and private sector facilities. The new system is mainly financed through social insurance contributions from employers and employees, with the government paying premiums on behalf of the poor. The Ministry of Health (MoH) is the main provider of health services, providing primary, secondary and tertiary care through its facilities nationwide.

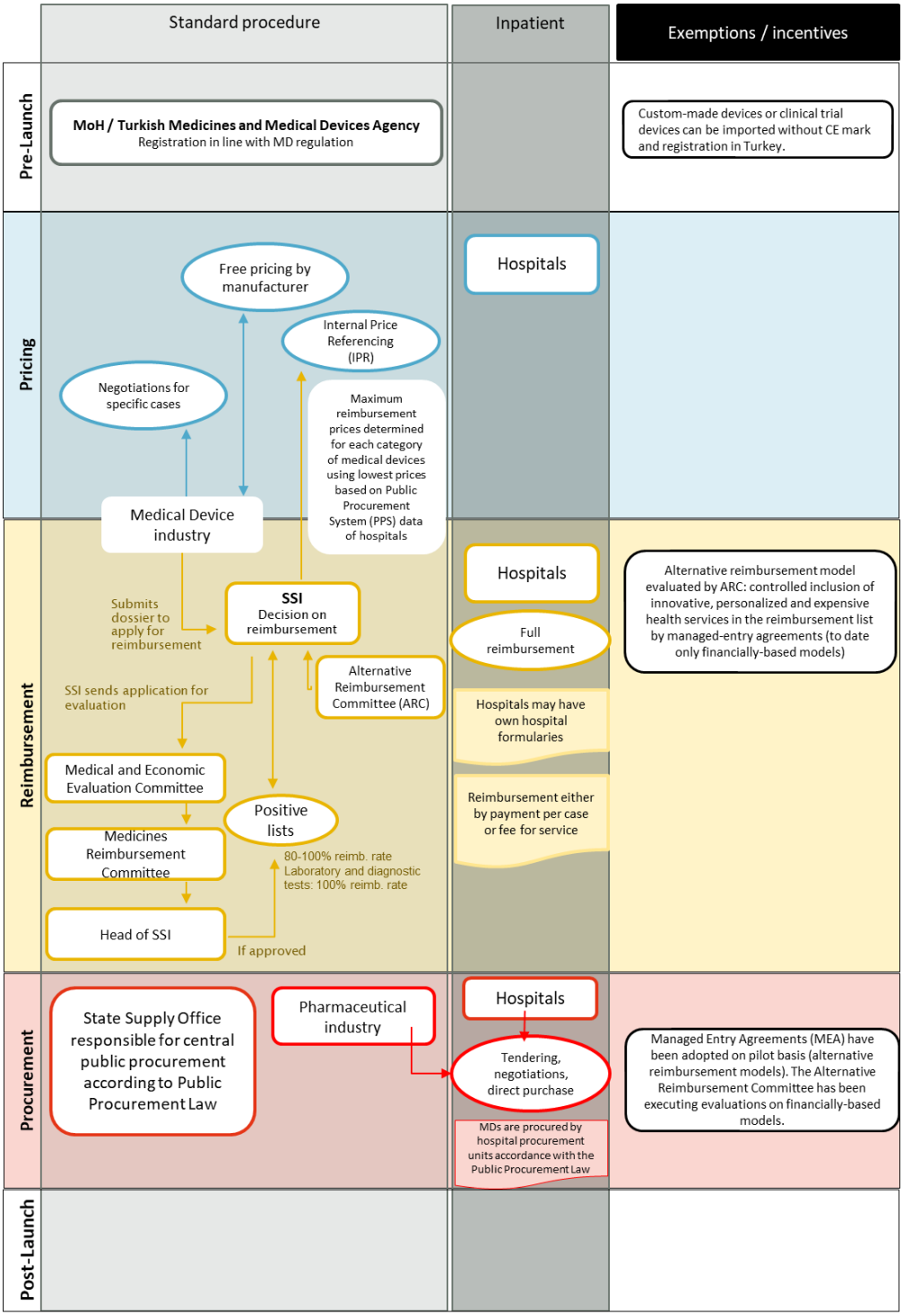
As the key regulatory authority, the MoH issues necessary regulations and oversees the pharmaceutical sector through its independent institution, the Turkish Medicines and Medical Device Agency (TITCK). While the SSI is the responsible authority for the implementation of the reimbursement system, the TITCK is in charge of almost all other aspects of medicines and medical device regulation, including marketing authorisation, production, pricing, import/export, clinical trials, distribution and safety monitoring.

Policy framework for medicines



Source: GÖ FP survey

Policy framework for medical devices



Source: GÖ FP survey

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7.3 Glossary

The glossary mainly contains terms related to reimbursement, pricing and procurement of health technologies. It is not a glossary on AMR.

Biosimilar (medicine)	A biological medicine that is developed to be similar to an existing biological medicine (the "reference medicine"). Biosimilar medicines can only be marketed following the patent expiry of the reference medicine.
Claw-back	A policy where funds already paid by public payers to pharmaceutical companies, wholesalers or pharmacists have to be paid back to the third party payers under certain conditions (e.g. if a certain threshold is exceeded).
Conditional pricing	A pricing policy that links the price of a health technology to specific conditions (e.g. health outcomes, minimum purchases). Conditional pricing is one type of a managed-entry agreement.
Co-payment	Patient's contribution towards the cost of a health technology covered by the insurer. Can be expressed as a percentage of the total cost of the health technology (percentage co-payment), as a fixed amount (e.g. prescription fee) or a deductible (=initial expense up to a fixed amount which must be paid out-of pocket for a health technology or over a defined period of time by an insured person; then all or a percentage of the rest of the cost is covered by a third party payer).
Cost-plus pricing	A pricing policy that takes into account production costs, promotional expenses, research & development, administration costs, overheads and a profit to determine a price.
Delisting	Exclusion of a health technology from a reimbursement list (e.g. positive list), often resulting in exclusion from reimbursement
Diagnosis-related groups (DRG)	A classification system of hospital cases used to pay hospital services, regardless of the cost to the hospital to provide services. The system is based not on the severity of the disease but on the amount of resources consumed.
Discount	A price reduction granted to specified purchasers under specific conditions prior to purchase.
Dynamic purchasing system (DPS)	An electronic framework agreement, which is completely run as an electronic process, in which new suppliers can join at any time.
External price referencing (EPR)	The practice of using the price(s) of a health technology in one or several countries in order to derive a benchmark or reference price for the purposes of setting or negotiating the price of the product in a given country.
Free pricing	Pricing policy, in which governments allow suppliers to determine the price of the medicine they launch.
Generic (medicine)	A medicine which has the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicine, and whose bioequivalence with the reference medicine has been demonstrated by appropriate bioavailability studies.

Health technology	Medicines, medical devices such as artificial hip joints, diagnostic techniques, surgical procedures, health promotion activities (e.g. the role of diet versus medicines in disease management) and other therapeutic interventions.
Health technology assessment (HTA)	A multidisciplinary process that summarizes information about the medical, social, economic and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, robust manner.
Horizon scanning	The 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.
Internal price referencing (IPR)	The practice of using the price(s) of identical or similar health technologies in a country in order to derive a benchmark or reference price for the purposes of setting or negotiating the price or reimbursement of the product in a given country.
Joint procurement	Procurement of certain products or services is done by a single purchasing body for several healthcare providers (e.g. hospitals, regions, countries).
Managed-entry agreement	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 and are usually classified into financial-based and performance-based MEA. Types of managed-entry include Access with Evidence Development, conditional coverage, Coverage with Evidence Development (CED), outcome guarantees, performance based agreement, price-volume agreements and risk sharing schemes.
Margin	The percentage of the selling price that is profit (e.g. a wholesale margin as a percentage of the wholesale price and a pharmacy margin as a percentage of the pharmacy retail price)
Marketing authorisation	A licence issued by a medicines agency approving a medicine for market use based on a determination by authorities that the medicine meets the requirements of quality, safety and efficacy for human use in therapeutic treatment.
Mark-up	The percentage of the purchasing price added on to get the selling price (e.g. a wholesale mark on the ex-factory price, or a pharmacy mark-up on the wholesale price).
Medical device	Any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, including the software intended by its manufacturer to be used specifically for diagnostic and/or therapeutic purposes and necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of: diagnosis, prevention, monitoring, treatment or alleviation of disease, diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap, investigation, replacement or modification of the anatomy or of a physiological process, control of conception, and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means.

Medicine	Any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis.
Negative list	A list of medicines or medical devices which are not included in the reimbursement scheme
Out-of-pocket (OOP) payments	The expenses of a person for health technologies that are not covered by reimbursement of a third party payer – often for a defined period (e.g a year). They include: » Expenses for non-reimbursable health technologies » Any form of co-payment to reimbursable health technologies, e.g. prescription fee, percentage co-payment, deductible
Peri-launch activities	Policies undertaken around the launch of a health technology on the market. Related to the entry of new medicines, this might be specific arrangements (e.g. managed-entry agreements, HTA) during the pricing and reimbursement decision process. Peri-launch activities address, among other things, issues of access and affordability.
Positive list (formulary)	A list of medicines and medical devices that may be prescribed, dispensed and used at the expense of a third-party payer
Post-launch activities	Policies undertaken after the launch of a health technology on the market. Related to the entry of new medicines, post-launch activities include monitoring the effectiveness and safety of new medicines in clinical practice and ensuring that patients with the greatest clinical need and those most likely to benefit from treatment can access the medicine, and include systematic detailed analysis of medicine usage data. Systems that facilitate data management include electronic accessible patient registries that collect key clinical data and e-prescription for reviewing prescribing practices to ensure these are consistent with agreed best practice outlines in guidelines and any prescribing restrictions.
Pre-launch activities	Policies undertaken before the launch of a health technologies on the market. This includes the review of the potential specific clinical and treatment outcomes and health system impact (in terms of cost and benefit to patients). Pre-launch activities also anticipate the budget impact and include horizon scanning and demand forecasting.
Price negotiation	A pricing procedure, in which medicine prices are discussed and agreed (e.g. between manufacturer and third party payer).
Price review	Evaluation of the price of all, or groups of, health technologies, typically in comparison to the prices of the same health technologies in other countries, in order to account for developments such as the market entry of medicines and price changes in other countries and exchange rate evolutions. Price reviews may, or may not, be performed in combination with reimbursement reviews. Price reviews can be done systematically (e.g. once a year) or irregularly.

Price type	The level (i.e. stage in the supply chain) at which the price of a health technology is set. Common price types include the ex-factory price, the pharmacy purchasing price (wholesale price) and the pharmacy retail price.
Pricing (price control, price regulation)	Action by a government authority to set the price of a health technology and/or indirectly influence it (e.g. through pricing policies) for different price types (e.g. ex-factory price, pharmacy retail price) and to monitor and review and eventually adapt it.
Procurement	A process to purchase goods and services (e.g. health technologies) that involves many steps and many stakeholders based on national, or supranational, regulation, policies, structures and procedures. An efficient procurement process must ensure that four strategic objectives are achieved: » the procurement of the most cost effective health technologies in the right quantities, » the selection of reliable suppliers of high-quality products, » procurement and distribution systems that ensure timely and undisturbed deliveries, and » processes that ensure the lowest possible total costs of procurement.
Rebate	A payment made to the purchaser after the transaction has occurred (ex-post discount).
Reimbursement (funding)	Coverage of the cost of reimbursable health technologies by a public payer (such as social health insurance/national health service NHS).
Reimbursement list	A list that contains health technologies with regard to their reimbursement status. They may either include medicines or medical devices eligible for reimbursement (positive list) or those explicitly excluded from reimbursement (negative list).
Reimbursement price	The maximum amount of a health technology paid for by a third party payer.
Reimbursement rate	The percentage share of the price of a health technology or medical service that is reimbursed/subsidized by a public payer. The difference between the reimbursed amount ("reimbursement price") and the full price of the health technology or medicinal service is paid by the patient (co-payment).
Reimbursement review	Evaluation process of a reimbursement decision (i.e. decision about the reimbursement status and reimbursement rates of health technologies), which may, or may not, include the price. Reimbursement reviews can be done systematically (e.g. once a year) for all reimbursed health technologies or a group (e.g. specific indication), or out-of-schedule.
Reimbursement status	Classification as to whether a health technology is eligible for reimbursement (reimbursable medicines) or not (non-reimbursable medicines).
Statutory pricing	Pricing procedure, where prices of a health technology are set on a regulatory basis (e.g. law, enactment, decree).
Tendering	Any formal and competitive procurement procedure through which tenders (offers) are requested, received and evaluated for the procurement of goods, works or services, and as a consequence an award is made to the tenderer whose tender/offer is the most advantageous.

Value-based pricing (VBP)	Through this policy authorities set the prices of a new health technology and/or decide on reimbursement based on the therapeutic value that a technology offers, usually assessed through health technology assessment (HTA) or economic evaluation. In a full-fledged VBP, the pricing and reimbursement systems are integrated, and the price and reimbursement decision is taken jointly based on a value assessment.
Value-based procurement	A procurement concept that is based on the on its longer term overall value rather than on its up front cost. It is supported by the "Most Economically Advantageous Tender" approach (MEAT) which was defined in the 2014 EU Public Procurement Directive (2014/24).

Note: The Glossary of Pharmaceutical Terms mainly relates to medicines. Adjustments were mainly performed to extend the terminology to further health technologies, including medical devices.
Fields with terms that specifically relate to the policy area of reimbursement, pricing and procurement are shaded in the respective colours (orange, blue and light red). The other fields are not shaded.

Source: Definitions based on the Glossary of Pharmaceutical Terms and Glossary of the PPRI Report 2018 [65, 74], for value-based procurement cf. Euriphi [120], adjusted and extended by the authors