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Pharmaceutical pricing and reimbursement in the Middle East and North Africa region

A mapping of the current landscape and options for the future

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Abbreviations

AED	United Arab Emirates Dirham
API	Active Pharmaceutical Ingredient
ATC	Anatomical Therapeutic Chemical (ATC)
BNF	British National Formulary
CCBA	Comparative Clinical Benefit Assessment
CCHI	Council of Cooperative Health Insurance (Saudi Arabia)
CIF	Cost Insurance and Freight
CNOPS	National Fund for Social Welfare Organisation (Morocco)
COO	Country of Origin
ERP	External Reference Pricing
FOB	Free on Board
GCC	Gulf Cooperation Council
GDP	Gross Domestic Product
GHC	Gulf Health Council
HTA	Health Technology Assessment
INN	International Non-proprietary Name
IRP	Internal Reference Pricing
ISPOR	International Society for Pharmacoeconomics and Outcomes Research
JFDA	Jordan Food and Drug Administration
JUH	Jordan University Hospital
KSA	Kingdom of Saudi Arabia
KAUH	King Abdullah University Hospital (Jordan)
MAD	Moroccan Dirham
MENA	Middle East & North Africa
MoH	Ministry of Health
MSP	Manufacturer Selling Price
MRP	Maximum Reference Price
NCD	Non-Communicable Diseases
NHRA	National Health Regulatory Authority (Bahrain)
NSSF	National Social Security Fund (Lebanon)
NUPCO	National Unified Procurement Company (Saudi Arabia)
OOP	Out-of-pocket
OTC	Over-the-Counter (medications)
PHI	Private Health Insurance
PPP	Purchasing Power Parity
R&D	Research and Development
RMS	Royal Medical Services
RSA	Risk Sharing Agreement
Rx	Prescription (medications)
SFDA	Saudi Food and Drug Authority (Saudi Arabia)
SHI	Social Health Insurance
SLR	Systematic Literature Review
TDL	Tender Drug List

UAE	United Arab Emirates
UHC	Universal Health Cover
USD	United States Dollar
VAT	Value-Added Tax
VBP	Value Based Pricing
WHO	World Health Organization

Executive summary

I. Background

Epidemiology, health care coverage and cost challenges change the healthcare environment and, unavoidably, pharmaceutical care, in the Middle East and North Africa (MENA) region. The focus is increasingly on health care and, predominantly, pharmaceutical cost containment, rather than efficiency improvements and reward for value.

The MENA geographical region includes countries with diverse economic status and health care systems – often very fragmented - and the application of health economic methods for health policy decisions, such as Health Technology Assessment (HTA) prior to pricing and reimbursement of pharmaceuticals and innovative contracting, is much less advanced compared to other geographical areas. While all countries are looking to reform their health systems, there is still room for significant improvement in order to streamline often fragmented systems and improve access to care and population health outcomes.

This report outlines and critically analyses the current pharmaceutical pricing and reimbursement policies and regulation in the MENA region and pays special attention to External Reference Pricing (ERP), the most commonly used pricing policy in the region. The focus of the report is on 11 countries: Algeria, Egypt, Morocco, Lebanon, Jordan, Saudi Arabia and the rest of the Gulf Cooperation Council (GCC) countries: Kuwait, United Arab Emirates (UAE), Qatar, Bahrain and Oman. Beyond mapping, analysing and critically appraising local pricing and reimbursement policies for pharmaceuticals and their interaction with each other, the report aims to recommend ways of improving current policies and practices and outlining a transition to a more robust value-based pricing system in the study countries. In doing so, the report also aims to motivate a positive dialogue around pricing, reimbursement and sustainability in the MENA region, as well as around the shared interest of patient access to medicines.

II. Methods

A methodological framework was created dividing the subject matter of the report into 5 groups: a) Pharmaceutical Pricing Policies; b) (explicit focus on) External Reference Pricing (ERP) and its salient features; c) Pharmaceutical Coverage & Reimbursement Policies; d) Spillover Effects of Pricing Policies; and e) Industrial Policies: Support for local and foreign manufacturers. Data collection informing the report was based on both (a) a systematic literature review (SLR), and (b) primary data collection from a variety of competent authorities and experts in the eleven study countries. The evidence was synthesised based on the above methodological framework, while an assessment of external reference pricing was performed using a validated methodological framework of 14 performance indicators relating to the good practice, notably: 1) Clear objectives of the ERP system; 2) ERP focusing on in-patent products; 3) ERP-derived prices not to override HTA or VPB; 4) ERP system to be administrative simple and transparent; 5) Stakeholders to participate in design and review of ERP system; 6) Stakeholders to be able to appeal; 7) Reference countries to be selected based on similarities in economic status and health system objectives; 8) International implications of ERP implementation to be considered; 9) Decisions to be made on publicly available ex-factory prices; 10) Mean prices to be also used; 11) ERP system to respect patent status; 12) ERP formula to avoid the impact of exchange rate volatility; 13) Price revisions to be kept to a minimum; and 14) ERP-based prices to be aligned with other tools used when negotiating reimbursement.

III. Pharmaceutical pricing policies in the MENA region and related issues

The health care environment and pharmaceutical coverage. Universal health coverage (UHC) (esp. in terms of services and level of coverage) varies significantly in the MENA region and ranges from 30% - 88%. Populous countries such as Egypt and Morocco have incomplete health insurance coverage and a significant part of pharmaceutical expenditure is paid for out of pocket. Coverage is often very fragmented with significant inequities among different population segments. Elsewhere (e.g. UAE or Saudi Arabia), where coverage of most key services has been good and free of charge for citizens, decision makers realise that a formalisation of the benefits package and the award of the same eligibility rights across different segments of the population requires significant attention, investment and policy intervention.

The dominance of ERP. The dominant method of pricing for in-patent pharmaceuticals across the MENA region is ERP, but additional criteria may apply, for example, the product price in the country of origin, the prices in the GCC region, the prices in official reference sources, such as the British National Formulary (BNF), when available, and the prices of pharmaceuticals in the same therapeutic category (internal reference pricing – IRP). In 2014, GCC countries implemented a unified pricing policy, setting a single price within the region to control pharmaceutical prices and contain pharmaceutical spending. The key objective of ERP currently is to serve as a cost minimisation tool in MENA countries by benchmarking against the lowest list prices from inherently diverse and large baskets.

Large ERP baskets. Reference baskets in the MENA region tend to vary from small baskets such as in Qatar, Kuwait and Oman, which reference the GCC region, to very large baskets such as those in Egypt and Saudi Arabia. The larger the basket, the more complex it becomes to administer an ERP system and the longer the delays in launching new products this practice may be associated with. Additionally, as the reference price for newly launched pharmaceutical products is calculated based on the lowest price in the basket, pharmaceutical prices converge downwards over time.

ERP administrative complexity. In its simplest form, ERP is not an administratively complex system. Nevertheless, primary research suggests that the administrative process is quite complicated and resource intensive, and that complexity is also directly related to the size of baskets and the frequency of re-pricing. Therefore, it is the intensity of information required often makes ERP schemes administratively complex. Additionally, while it is important to ensure that ERP systems are transparent, rebated or discounted prices are sometimes used, and these are not fully transparent and, therefore, not defensible before the stakeholder community.

EPR and value assessment. In the majority of cases, the operation of an ERP scheme does not account for the value of innovation. For instance, an issue arises when ERP is combined with molecular or therapeutic price referencing, the latter being a frequently-used option setting a reference price across a range of molecules, of which at least one is patent-expired. It is likely that these two effects can be combined and can spill-over across borders. Additionally, it is important to have in mind that the value of innovation could not be considered without proper generation of local data, such as burden of disease, incidence and prevalence. In that context, capability and capacity building is also an important component.

ERP and exchange rates. Appropriate exchange rates are also essential in ensuring realistic prices rather than prices arising from excessive exchange rate volatility, and

particularly depreciation, which can also lead to product shortages on the market (Egypt has suffered on this front fairly intensely over the past year due to the depreciation of the Egyptian pound).

ERP and spill-over effects. The way in which ERP is implemented in a country might have an additional impact on the availability of pharmaceuticals. This is due to ERP policies, which are most likely to take place in highly regulated and/or small markets. ERP spillover effects are also common: from a policy perspective, ERP in itself does not restrict access once agreement has been reached but can lead to delays in launch, which, in itself can cause access problems. It can also be the case that manufacturers will not launch in a particular ERP market if they feel that the price they receive from that market is prohibitively low and can threaten their global pricing strategy.

ERP and best practice principles. None of the study countries in the region seemed to satify all 14 of the ERP best practice principles with most failing to use the mean price of the basket and an administratively simple and transparent system which involved stakeholder participation. Most countries use the lowest price in the basket, have large baskets, reducing administrative simplicity. Similarly, whilst external stakeholders may be consulted, their contribution to the actual decision making related to ERP is practically null, it is an administratively driven process that excludes active participation by stakeholders.

Lack of value assessment systems. There is no formal value assessment system in operation explicitly in any of the MENA countries along the lines of a Health Technology Assessment (HTA) system based on clinical and cost-effectiveness analysis or comparative clinical benefit assessment. These systems are still in an aspirational sphere for all the countries in the region, but there are trends, such as the recently passed legislation on UHC in Egypt and Saudi Arabia's Vision 2030, where mention is made on HTA and efficiency either explicitly (Egypt) or implicitly (Saudi Arabia).

Generic pricing. Prices of generics in the MENA region are usually set as a fixed percentage below the originator price (price capping), with prices varying from the first generic(s) to the following ones entering the market (managed competition). There are differences in the criteria in which locally manufactured pharmaceutical products are priced in the study countries, compared with imported pharmaceuticals (both brand and generic).

IV. Coverage and reimbursement policies and procurement in the MENA region and related issues

Fragmented reimbursement systems. Many of the countries in the MENA region have fragmented reimbursement systems with many actors involved in the purchasing of medicines, delivery of healthcare, and reimbursement mechanisms. Bahrain, Kuwait Saudi Arabia, the UAE and Qatar have comprehensive healthcare coverage for their citizens. Most countries in the region rely on a combination of government funding, national health insurance schemes, and out-of-pocket (OOP) spending to fund their healthcare needs. Tendering is the most prevalent mechanism for the procurement of *off-patent and generic pharmaceuticals*. It is, however, often used in combination with other mechanisms, such as IRP, CBA and formulary management. Tendering is also widely used for the procurement of *in-patent pharmaceuticals* (Egypt, Jordan, Lebanon, Morocco, Saudi Arabia).

Procurement and reimbursement of medicines. The methods used for the procurement and reimbursement of in-patent drugs vary widely across the MENA region. Most countries employ a combination of mechanisms for reimbursement decisions, such as tendering and formulary management. More recently, reimbursed prices of in-patent

medicines – particularly very innovative ones that also carry a significant financial burden for health systems – have been subject to negotiation with national competent authorities.

Risk sharing and HTA. The region has witnessed an increase in awareness on the use of financial-based risk-sharing agreements, although this is a very recent trend, which is yet to manifest itself in practice. There is a lack of formal value assessment through Health Technology Assessment (HTA), although some countries are using some form of comparative clinical benefit assessment combined with budget impact analysis or have a requirement for a 'token' cost-effectiveness study to be submitted for consideration by the competent authorities (Algeria, Morocco, Lebanon). Formal use of HTA is still some way off and the most tangible example of willingness to move forward in that direction is Egypt through the enactment of UHC in spring 2018, which makes explicit reference to HTA.

Reimbursement practices and availability. Conducting tenders is key in ensuring coverage across MENA countries. Public sector procurement is sometimes performed through independent annual tenders (rather than being unified or joint across health care organisations/insurers) and can lead to double purchasing whereby the government pays for more than one public health organisation purchasing the same pharmaceutical in the same year at distinct prices. An obvious solution in this context would be joint or unified procurement, which was implemented in the case at hand.

Despite the increased interest in the use of HTA and risk sharing agreements (RSAs), neither tool is used in the MENA countries' reimbursement systems, nor are there independent or quasi-independent institutions tasked with the conduct of HTA (whether this is on the clinical cost effectiveness or the comparative clinical benefit assessment analysis). Beyond efforts to move into the direction of HTA in the future in two countries (Egypt, Saudi Arabia), in some cases (Egypt, Lebanon), there are requirements to submit economic analysis (e.g. budget impact) aiming to aid negotiations with manufacturers, particularly on expensive innovative products. The experience with and implementation of RSAs are also very limited with the exception of some recent attempts featuring expensive, innovative products for rare diseases (Algeria, Egypt, Lebanon).

ERP is not used as a reimbursement tool in the MENA region. However, in several countries, ERP prices set in the pricing process become the starting point for negotiations or other reimbursement methods and often, ERP prices become reimbursement prices.

The role of demand-side measures in pharmaceutical policy. There is a larger effort towards implementing mandatory generic prescribing, however, none of the countries has implemented an electronic system to manage and make generic prescribing mandatory. In addition, while most countries in the region have a generic substitution policy, it has only been made mandatory practice in Jordan. This trend is also linked to the relative lack of compulsion in the use of generic medicines – where possible - in order to improve affordability.

V. Local industrial policies

Across the study countries, there seems to be significantly more support provided to domestic than to foreign manufacturing entities. Support for domestic manufacturers is predominantly through pricing and reimbursement policies which may discriminate against multinational manufacturers, in terms of tax regimes, import duties or preferential treatment in public procurement. The most commonly provided support, is public procurement which often gives preference, including price advantages, to local manufacturers. On the other hand, foreign manufacturers receive support mostly through

taxation or subsidy incentives, which are not necessarily tailored for the pharmaceutical sector but apply generally.

VI. Impact of pricing, reimbursement and procurement policies in the MENA region

The impact of pricing policies in the MENA region has been significant, and mostly relates to: a) Prices in the region; b) Access Barriers and Availability Concerns; c) Affordability issues; and d) International implications.

Prices. With regards to prices, the evidence generally indicates, that ERP and the way it is structured and implemented, delivers low pharmaceutical prices in the MENA region by international standards. However, the impact of ERP can be quite distorting as it creates artificial benchmarks, which are not necessarily linked to tangible or robust local assessment systems. As a result, ERP may not be the optimum pricing policy for achieving competitive and appropriate price levels, compared to a more dynamic pricing policy which allows pharmaceuticals to express value in their national context.

Access Barriers and Availability Concerns. A country's pricing policy, its degree of inflexibility and the length of the negotiation process can indirectly impact pharmaceutical availability through influencing the price levels a manufacturer can achieve in that country, thereby impacting their decision to launch and/or withdraw a product in/from a market. Although there is limited quantifiable evidence, there has been some evidence of product shortages in some of the study countries.

Affordability issues. Pharmaceutical affordability is an issue of varying importance across the MENA region as prescription drug coverage is partial and the out-of-pocket burden for citizens is often high. There are many factors influencing or shaping pharmaceutical affordability, including the pharmaceutical pricing framework, the level of coverage and the extent of the drug benefit provided by the health care system. As such, affordability is inexorably linked to the way medicines are reimbursed and the methods that are used to ensure that reimbursed prices are affordable. If, as appears to be the case in the majority of MENA countries, the ERP is a price that is reimbursed by the countries concerned without further action on reimbursement negotiation, then, unavoidably, questions arise about the extent to which such prices are affordable.

International implications of ERP. Given the nature of ERP, international implications such as spill-over effects in third countries, are to be expected. The evidence on international implications and their impact is presented as three key issues: (a) spill-over impact of ERP to third countries in terms of launch delays, which affect availability in the countries in the region; (b) the effect of ERP on third countries in terms of price convergence and the direction of the convergence, which in most cases is shown to be downward; and (c) whether the decision-making community is aware of the international implications of ERP, and if so, their response to them; in this case, evidence suggests that with very few exceptions, there is little awareness about the international implications of ERP.

VII. Policy options for the future

There are three broad sets of policy options for the future with regards to pharmaceutical pricing and reimbursement. The first reflects on the peculiarities of ERP and how the current system as is implemented in different MENA countries can be calibrated to a more effective and efficient tool over the mid- to long-term; the second reflects on how the

limitations of current systems of coverage and reimbursement can be overcome and what the requirements are for the establishment of more formalised arrangements around value assessment that will rely on local assessment of evidence rather than simply borrowing prices from other settings; and the third relates to UHC and the implications for pharmaceutical reimbursement.

(1) Optimising ERP systems

Is ERP serving the objective of cost minimisation and efficiency improvements? Increasingly, the objectives of cost minimisation and efficiency improvements cannot be met through ERP as list prices for many or most new products are no longer representative of net or transaction prices in most reference countries that MENA use as reference. This is due to RSAs, confidential discounting and negotiations between pharmaceutical companies and competent authorities in the reference countries. Consequently, in most reference countries the fundamental objective in the use of ERP has shifted from a cost minimization tool to a tool that guides negotiations for affordable prices.

The use of ERP in the future. Countries in the MENA region have been implementing ERP for several years now, but, over time, it has become obvious that ERP in itself poses significant limitations to early access. ERP is also limited because it is increasingly associated with artificial list prices in many (if not most of) the settings MENA countries are using as reference. It has become clear, therefore, that ERP may be *one of* the steps needed to arrive at affordable prices rather than the *only* step. Even countries in other settings that have traditionally relied on ERP to determine prices in their territory and negotiate reimbursement rates, are increasingly using ERP as one of the (less important) criteria to achieve their goal. As such, ERP is a supplement to a range of tools that are used to arrive at affordability, including an explicit value assessment, through HTA principles, and the implementation of RSAs, where this is feasible. Consequently, ERP should in principle provide the starting point for negotiations regarding the reimbursability of new products and their inclusion into national benefits' catalogues. MENA countries can continue to implement ERP in the future as well as strive to adhere as much as possible to the ERP best practice principles, but safeguard affordability not by resorting to the lowest price in extensive ERP baskets, but by implementing competent negotiation strategies and value assessment methods. Additionally, and to the extent ERP continues to be implemented, it is necessary to maintain a confidential net pricing system which will allow competent authorities and manufacturers to negotiate based on the formers' needs.

Calibrating ERP. The analysis using the framework of the 14 best practice principles in the MENA countries may suggest a number of ways forward, with both medium- and long-term perspective. MENA decision-makers can optimise ERP systems in the medium-term by intervening constructively and refining certain elements that are further away from best practice. Priority should be given to the following elements: (a) improvements in administrative simplicity, (b) the existence of robust appeals mechanisms, (c) the selection of reference countries in the sample, (d) recognising and accounting for the international implications of ERP, (e) using publicly available ex-factory prices to shape list prices, (f) using mean (or at least median) prices rather than lowest and (g) avoiding the exploitation of exchange rate fluctuations. Countries such as the UAE and Saudi Arabia have made significant inroads in the past few years towards an improved ERP system.

The long-term interventions by MENA decision-makers in the context of improving their ERP systems relate to (a) the clear (re-)alignment of ERP objectives with health system objectives, (b) the exclusive focus of ERP on in-patent products, (c) the fact that ERP should not override HTA or alternative approaches (e.g. Value-based pricing (VBP)), (d)

the respect of patent status and (e) the alignment of ERP-based prices with other tools used when negotiating reimbursement. These principles and the associated options are discussed further in the paragraphs that follow.

(2) Transitioning from ERP to value-based pricing (VBP)

International developments in value assessment. From an international standpoint, over the past 15 years, the focus has shifted from ERP to (a) the establishment of robust criteria for value assessment based on clinical and/or economic evidence, (b) the introduction of HTA, (c) the consideration of additional criteria beyond costs and effects, which capture the importance of the local context and local data such as burden of disease, incidence, prevalence and severity, (d) the use of negotiation principles to arrive at reasonable and affordable prices and (e) the more extensive use of risk sharing principles to inform local coverage decisions. Important country examples include Spain (where ERP's importance has declined significantly over the past decade in favour of comparative clinical benefit assessment), Italy (completely departed from the principle of average European price to implement HTA, negotiation and extensive risk-sharing), Poland (abandoned ERP and using HTA with a fixed threshold to inform pricing and coverage decisions), Belgium (abandoned ERP in favour of a direct negotiation model based on clinical value assessment and extensive risk sharing), and, more recently, Greece (where the establishment of HTA and direct negotiation with risk sharing will become the dominant model in the future). Outside Europe, important is the experience of Brazil and South Korea in the same vein, while countries such as Turkey are using some kind of HTA and have alternative mechanisms to deal with novel and expensive therapies in a way different than what ERP principles postulate.

Requirements for the transition to a more formalised value assessment system. The transition to more formalised models of value assessment can be made possible through investment in three key areas: first, significant investment is required in institution-building, such that there are new competent authorities and institutions to address the challenges of modern value assessment; second, significant investment is required in human capital and development of capabilities that are necessary to address the above challenges; third, investment in data generation processes in order to ensure that whatever decisions are made, can be made on the basis of robust and validated evidence. To an extent, the focus on institutions and human capital determines the roadmap that needs to be followed; evidence from settings that have already progressed to a formal value assessment system suggests that transitioning from one model to another cannot be made overnight but that the long-term benefits for local health care systems can be significant, esp. in the context of UHC.

The likely role of HTA in value assessment in the MENA region. HTA can play the role of a catalyst in key MENA markets. The implementation of HTA has so far escaped the MENA region, but there are signs that HTA and value assessment are likely to be implemented in some form in countries such as Egypt and Saudi Arabia in the years to come. Agreement on best practices is important because HTA is increasingly a fundamental part of the way organisations decide on which health technologies they will reimburse. Equally, the implementation of HTA principles, requires a gradual shift in policy-making towards an environment which is more transparent, collaborative, consultative and is supportive of innovation and investment.

Before even considering HTA adoption, a set of prior actions are needed in order to prepare the ground, as follows: (a) interested countries should think how it will be incorporated in their decision-making processes, including the interaction with other policy tools, such as

ERP; (b) a decision to adopt HTA should be followed by investment in human and physical infrastructure as well as data systems to support its implementation; (c) a period of learning is also desirable; (d) if HTA is established, it needs to be separated from the registration process and should not impact registration based on efficacy and safety; (e) the principles of HTA should ultimately be applied across a wide range of medical interventions, rather than medicines only. Beyond these prior actions, interested countries should carefully consider (a) all available options around an *HTA system* and select one that satisfies their interests before deciding to adopt one; and (b) all available options around an HTA model, before deciding to adopt one. All the above should take place in a stepwise manner.

(3) Re-thinking universal health coverage and reimbursement

Fragmented vs. unitary reimbursement systems. Given the gaps in health coverage and service provision, the goal of UHC (and its implications for the pharmaceutical market) will most likely need to be the focus of policy attention over the next decade or so. Unavoidably, this impacts pharmaceutical reimbursement. The transition from fragmented reimbursement systems in individual countries, based on employment status or type of employment (e.g. government employees or military personnel), to a 'unitary' or single reimbursement system with the same principles across all citizens is desirable on equity, efficiency and effectiveness grounds. It will also require significant attention, investment as well as adherence to strict budgetary and efficiency principles.

Supply- and demand-side policy foci on reimbursement. The likely shift towards unitary reimbursement systems, is likely to have implications for all components of the pharmaceutical value chain from the top end of the market, where the focus is on value assessment of new and innovative treatments and their timely incorporation into the benefits catalogue, to the lower end of the market, where there needs to be a more robust and consistent generics policy, both from a supply-side (pricing and price setting) and a demand-side (prescribing, dispensing, cost-sharing) perspective. A sound framework that ensures the quality of generic medicines is an absolute pre-requisite in this context. Beyond generating 'unitary' reimbursement systems, national pharmaceutical policies will need to address the issue of financing and its sustainability, a balanced industrial policy, the regulation of the distribution chain, and the assessment of policy interventions.

1. Introduction

The healthcare environment in the Middle East & North Africa (MENA) region is subject to considerable change, both in terms of epidemiology and in terms of health care spending and coverage. In the Gulf Cooperation Council (GCC) region, for example, the average proportion of deaths attributable to non-communicable diseases (NCDs) approaches 70%, with Saudi Arabia and Kuwait recording rates above this average at 78% and 73% respectively (WHO, 2014, 2014a). In Egypt, with a population of 95.7 million, 82% of deaths are attributed to NCDs and where the prevalence of diabetes and hypertension stand at 17% and 40% respectively. The combination of NCD prevalence, economic and fiscal pressures, as well as national priorities in some countries to achieve universal health insurance provide a challenging environment for health care services and its components. Unavoidably, pharmaceutical care, as a very important, but readily identifiable, component proportionately is subject to the same challenges.

In this challenging context, pharmaceutical policy is increasingly becoming a subject of scrutiny in all countries in the region, where the focus is increasingly on health care and pharmaceutical cost containment, rather than efficiency and reward for value. One example of this focus relating to pharmaceuticals is the GCC Price Harmonisation Policy initiative, which was implemented as a mechanism to address price variability between GCC countries and reduce pharmaceutical prices. While the mid- to long-term impact of this policy on the market, on pharmaceutical companies, and the healthcare in the GCC in general remains to be seen, the pricing mechanism used in the setting of unified prices, whether for marketed products or future launch products is a subject for debate.

While all countries are looking to reform their health sector, there is still room for significant improvement in order to streamline fragmented sectors and improve access to care and population health outcomes. The MENA geographical region includes countries with diverse economic status and health care systems and the application of health economic methods for health policy decisions, such as Health Technology Assessment (HTA) prior to pricing and reimbursement of pharmaceuticals and innovative contracting, is much less advanced compared to other geographical areas.

This report outlines and critically analyses the current pricing and reimbursement policies, regulation and legislation in the MENA region and pays special attention to external reference pricing (ERP), which is the most commonly used pricing policy in the region. ERP is the practice of using the price of a medicine in one or several countries in order to derive a benchmark or reference price for the purpose of setting or negotiating the price of the product in a given country. Another fairly common pricing practice in the region is Internal

Reference Pricing (IRP), which is often combined with ERP. IRP consists of clustering drugs according to some equivalence criteria and defining a reference price for each cluster, particularly when patents have expired. There are three distinct types of clustering: a) Molecular reference pricing, where medicines with the same active substance (ATC-level 5) are grouped to define the reference price; b) Therapeutic reference pricing, where all drugs that are used to treat a particular condition or medicines that have a comparable therapeutic effect (ATC-level 3) are grouped to define the reference price; and c) Managed competition in combination with molecular reference pricing, which combines molecular reference pricing and a price cut for additional entrants with the same active substance.

By identifying and discussing trends in pharmaceutical pricing and reimbursement in the MENA region, with a focus on Algeria, Egypt, Jordan, Lebanon, Morocco, Saudi Arabia and the rest of the Gulf Cooperation Council countries: Bahrain, Kuwait, Oman, Qatar, and the United Arab Emirates (UAE) (the 'study countries'), the report aims to:

1) Map, describe, analyse and critically appraise local pricing and reimbursement policies for pharmaceuticals;
2) Describe and analyse the current use of ERP systems, their modalities and implementation, as well as their interaction with other pharmaceutical policies and practices in the countries concerned;
3) Identify local best practices that can be shared effectively across the region, recommend ways to improve current interventions, and outline a transition to a more robust value-based pricing system in the study countries; and
4) Motivate a positive dialogue around pricing, reimbursement and sustainability in the MENA region, as well as around the shared interest of patient access to medicines.

To achieve these aims, in this report we have applied a three-step approach comprising (a) a systematic literature review (SLR), (b) primary data collection from a variety of competent authorities in the eleven study countries and (c) an analysis utilising the primary and secondary evidence collected, as well as a validated methodological framework of 14 performance indicators relating to the good practice in the introduction and use of ERP.

The report is structured as follows: Section 2 outlines the methodology employed, discussing the parameters for the systematic literature review, the primary data collection, and the analysis conducted to address the objectives of the paper; Section 3 summarises key trends in health and pharmaceutical care spending and funding sources; Section 4 outlines the key pricing policies for in-patent, off-patent, and generic pharmaceuticals across the study countries, together with a review of the role and features of ERP; Section

5 presents the key mechanisms for procurement and reimbursement across the study countries; Section 6 outlines findings on industrial policies or practices in support of either local or foreign companies. Section 7 discusses the impact of pricing, reimbursement and industrial policies across four key endpoints: price levels, access barriers, affordability, and international implications. Finally, Section 8 presents a number of policy options for the future.

2. Methodology

2.1. Analytical framework

The evidence informing the report comes from both primary and secondary sources. In order to address the report objectives, we created an analytical framework with associated endpoints, which were separated into five groups: a) Pharmaceutical Pricing Policies; b) (explicit focus on) External Reference Pricing (ERP) and its Salient Features; c) Pharmaceutical Coverage & Reimbursement Policies; d) Spillover Effects of Pricing Policies; and e) Industrial Policies: Support for local and foreign manufacturers. The identified endpoints are shown in **Table 1** alongside brief definitions.

2.2. Systematic literature review

We conducted a systematic literature review (SLR) in order to map available evidence on pricing and reimbursement policies in the study countries and identify the possible impact of these policies. The SLR was based on an extensive review of both peer-reviewed and grey literature on the pharmaceutical pricing and reimbursement trends in study countries, with the aim to provide an accurate picture of the current landscape based on the analytical framework discussed above. A detailed search strategy for the SLR and the literature identified can be found in **Appendix 1**.

Table 1: Analytical framework and key endpoints

Key Themes of Analytical Framework	Key indicators/endpoints	Aim of framework theme and associated indicators
Pharmaceutical Pricing Policies	▪ Pricing policies for in-patent pharmaceuticals ▪ Pricing policies for off-patent pharmaceuticals ▪ Pricing policies for generic pharmaceuticals ▪ Pricing policies for locally manufactured pharmaceuticals ▪ Pricing policies for imported pharmaceuticals	Discusses current approaches to pricing and the extent to which they differ between different types of pharmaceutical products.
External Reference Pricing (ERP): Salient features	▪ Time ERP was introduced and responsible authority ▪ Role of ERP: a) Is it used for pricing and/or reimbursement? b) Does it have a supportive or main role in price setting? ▪ Basket of countries a) Number of countries b) Countries c) Selection criteria for basket countries ▪ Price used to inform pricing decisions ▪ Information sources for identification and validation of ERP prices ▪ Reference price calculation ▪ Price revisions	Reflects on the salient features of the prevailing ERP model, as the dominant method of pharmaceutical pricing, in order to identify similarities and differences across study countries in the way ERP is implemented across the region.
Pharmaceutical Coverage & Reimbursement Policies	▪ Pharmaceutical financing: a) Government b) National health insurance c) Private health insurance d) Out Of Pocket (OOP) payments ▪ Coverage Policies ▪ In-patent pharmaceuticals ▪ Off-patent/generic pharmaceuticals ▪ How ERP is used to shape coverage/reimbursement ▪ Incentives that ERP provides to improve efficient purchasing, incl. prescribing and procurement ▪ Generic prescribing and substitution	Identifies the sources of finance for pharmaceutical products, the extent of OOPs and any supply- and demand-side policies relating to pharmaceutical coverage.
	▪ Price levels	Examines the impact of pricing and reimbursement policies on pharmaceutical price levels, and whether pricing policies lead

Spillover Effects of Pricing Policies		to or can achieve acceptable prices for payers of health care in the MENA countries.
	▪ Drug product shortages	
	▪ Access barriers	Assesses the extent to which pharmaceuticals are available on a timely basis, and with limited access barriers in the MENA countries.
	▪ Affordability issues	Examines whether pharmaceutical prices are aligned with the purchasing ability of patients and/or health care systems.
	▪ International implications	It assesses the extent to which there are spill-over effects of ERP to third countries in terms of (a) launch delays, and (b) price convergence.
Industrial Policies: Support for local and multinational manufacturers	▪ Support of local industry: Pricing incentives, tax breaks/exemptions, discounts, tendering/procurement, discounts, price caps ▪ Support of foreign/research-based industry: Pricing incentives, tax breaks/exemptions	Analyses the degree to which the adopted pricing policies promote and/or are aligned to industrial policy objectives. Specifically, it examines whether the support provided to local and multinational manufacturers respectively, promotes industrial policy objectives or whether it acts as a barrier to achieving these. The objectives of industrial policy focus on effective entry and market penetration of generic pharmaceuticals, incentives for manufacturing and/or R&D investment, and higher revenues for manufacturers.

Source: The authors.

2.3. Primary data collection

To complement our literature search and validate our findings, while also incorporating local insights to pinpoint regulatory challenges and derive recommendations, we also engaged in interviews with stakeholders across the study countries. This stage also informed the identification of gaps, barriers and bottlenecks throughout the mapping exercise materials. Responses were subsequently coded thematically in order to pull out key concepts and trends throughout the region.

We developed an Interview Discussion Guide (**Appendix 2**) which provided questions that were discussed during the interviews. The Interview Discussion Guide was designed according to the SLR endpoints and incorporated a validated methodological framework for ERP best practice. The Interview Discussion Guide comprised three sections: (a) Pricing policies and price setting; (b) Reimbursement and coverage decisions; and (c) Evidence of ERP impact within and across countries.

A glossary and a list of abbreviations were also created and distributed to the identified respondents in order to clarify terms used in the interview that interviewees were not immediately familiar with. Over 80 local experts and stakeholders were contacted; these included government officials, representatives from regulatory authorities, insurance organizations, pharmacy departments, and procurement agencies, among others, but also industry executives. Of these, 31 experts contributed material, insights and information that fed into this report. The list of interviewees and their affiliations is shown in **Appendix 3**. An additional round of triangulation with local stakeholders took place during the ISPOR conference in Dubai in September 2018 by the lead author and aimed at validating many of the original findings in face-to-face meetings with several experts from competent authorities.

2.4. Analysis

Based on the SLR results and the primary data collection, an analysis was undertaken focusing on: (a) mapping, outlining and discussing current pricing and reimbursement policies in the study countries; (b) outlining practical issues and challenges in the implementation of the widely used EPR in the study countries; and (b) offering practical suggestions on how to improve operational procedures in the transition from price-focused to value-focused policies.

The policy mapping consisted of detailed fact-files on a by endpoint and country-by-country basis based on the methodological approach outlined above. We assessed how well national ERP systems adhered to best practice by using a validated methodological

framework comprising 14 principles (Sullivan, Kanavos & Kalo, 2015) and endeavoured to showcase the performance of national ERP systems based on these principles; the principles are shown in **Table 2**.

Subsequently, the available evidence was critically appraised to arrive to a number of key policy recommendations regarding improvements in pharmaceutical pricing and reimbursement policies in the study countries, specifically as they relate to ERP and its operating environment. A qualitative assessment of the current situation in the study countries was conducted and a gradual departure from the EPR system towards more value-based approaches or a refinement of the conditions governing the implementation of EPR, were also explored based on the available evidence at country level.

Table 2: The 14 best practice principles of ERP

No.	ERP best practice principle
1	The objectives of ERP systems should be clear and align with health system objectives
2	ERP systems should focus on in-patent products considered for the purposes of coverage, pricing and reimbursement decisions
3	Prices developed via ERP do not override HTA conclusions or VBP approaches
4	The ERP system should have administrative simplicity and transparency
5	Stakeholders should participate in design and review of ERP system
6	Stakeholders are able to appeal regulator decisions
7	Reference countries should be selected based on similarities in economic status and health system objectives
8	International implications of ERP implementation should be considered
9	Publicly available ex-factory prices should form the basis of the ERP system
10	The mean of prices in reference countries should be used
11	ERP system respects patent status of products it covers based on provision of IP that prevail in reference country
12	ERP formula should avoid the impact of exchange rate volatility
13	Price revisions should be kept to a minimum and should be carried out consistently to avoid the perception of opportunistic behaviour
14	ERP-based prices should be aligned with other tools used when negotiating reimbursement

***Source**:* Sullivan, Kanavos & Kalo, 2015.

3. Healthcare and pharmaceutical spending

3.1. Healthcare expenditure and sources of financing

Table 3 provides an overview of the health financing and expenditure trends in the study countries. Current health expenditure ranges between 3.1% and 7.4% of GDP in the eleven MENA countries. Total health expenditure comprises the greatest proportion of GDP in Lebanon (7.4%), Algeria (7.1%), and Jordan (6.3%), and the lowest proportion of GDP in Qatar (3.1%), UAE (3.5%), and Oman (3.8%). Government health expenditure comprises between 1.25% and 4.98% of GDP in the study countries. Understandably, there is a significant difference between total and public (government) spend on health, and the difference is mostly covered through out-of-pocket (OOP) spending. Government health expenditure comprises the greatest proportion of GDP in Algeria (4.98%), Saudi Arabia (4.16%), and Lebanon (3.76%), and the lowest proportion of GDP in Egypt (1.25%), Morocco (2.39%), and UAE (2.47%). It may be unsurprising that government health expenditure comprises the highest proportion of GDP in Algeria, since Algeria's government health expenditure comprises 71% of current health expenditure, whereas private health expenditure comprises only 29% of current health expenditure. Equally it may be unsurprising that Egypt's government health expenditure comprises the lowest proportion of GDP, since Egypt's private health expenditure comprises 70% of current health expenditure, whereas government health expenditure comprises only 30% of current health expenditure.

There is considerable variation in the current health expenditure per capita between the eleven countries. In 2015, the eleven MENA countries' current health expenditure per capita, varied between 435.29 current international $ (PPP) in Morocco to 3,900.29 current international $ (PPP) in Qatar. Of the eleven countries, the six GCC states with a range between 1635.87 and 3900.29 current international $ (PPP), spend the most per capita on health. The GCC states' high per capita spending on health may be driven in part by the higher government involvement in the six states compared with the other MENA countries. Government expenditure in the six GCC states accounts for a higher proportion of current health expenditure than in the other MENA countries, except for Algeria.

Table 3: Health care expenditure and sources of health system financing, 2017 PPP$[1]

	Total Health Expenditure (2017 PPP$, bn)	Current Health Expenditure (% of GDP)	Current health expenditure per capita (current PPP$)	Domestic private health expenditure per capita (current PPP$[2])	Domestic private health expenditure (% current health expenditure)	Out-of-pocket expenditure per capita, PPP (current international $)	Out-of-pocket expenditure (% current health expenditure)	Domestic general government health expenditure per capita (current PPP$)	Domestic general government health expenditure (% of GDP)	Domestic general government health expenditure (% current health expenditure)	"External"[5] health expenditure per capita (current PPP$)	"External"[5] health expenditure (% current health expenditure)
Algeria	40.8	7.06	1,031.17	303.12	29.40	289.75	28.10	727.78	4.98	70.58	0.27	0.03
Bahrain	3.4	5.16	2,453.16	829.29	33.80	615.73	25.10	1,623.87	3.41	66.20	0.00[3]	0.00[3]
Egypt	43.7	4.17	495.17	344.96	69.66	306.80	61.96	148.95	1.25	30.08	1.26	0.25
Jordan	5.5	6.28	568.12	205.33	36.14	142.88	25.15	324.79	3.59	57.17	38.01	6.69
Lebanon	6.9	7.43	1,117.26	537.40	48.10	358.30	32.07	564.59	3.76	50.53	15.26	1.37
Morocco	15.1	5.53	435.29	242.52	55.71	231.07	53.08	188.46	2.39	43.29	4.31	0.99
Kuwait	10.1	4.03	2,977.51	473.30	15.90	428.13	14.38	2,504.21	3.39	84.10	0.00	0.00
Oman	7.7	3.83	1,635.87	192.16	11.75	104.14	6.37	1,443.72	3.38	88.25	0.00	0.00
Qatar	7.2	3.06	3,900.29	568.95	28.75	242.92	17.79	3,331.33	2.61	71.25	0.00[4]	0.00[4]
Saudi Arabia	97.3	5.83	3,121.34	895.39	28.69	467.58	14.98	2,225.95	4.16	71.31	0.00[3]	0.00[3]
UAE	23.6	3.47	2,425.80	697.39	28.75	431.54	17.79	1,728.41	2.47	71.25	0.00	0.00

Notes: [1] Adapted from 2015 national expenditure data.
[2] Domestic private health expenditure per capita in current PPP$ includes out-of-pocket expenditure per capita, in current PPP$.
[3] Adapted from 2014 national expenditure data.
[4] Adapted from 2013 national expenditure data.
[5] Relating to foreign aid.

Source: World Bank, except for total health expenditure data, which comes from Institute for Health Metrics and Evaluation (IHME), 2018.

Likewise, except for Bahrain, the six GCC states all spend a considerably lower proportion of current health expenditure on out-of-pocket payments.

We estimated that the ratio of total health expenditure to government health expenditure accounts for between 30% in Egypt and 88.3% in Oman; prepaid private health expenditure comprises between 1.3% in Algeria and 15.9% in Lebanon; out-of-pocket payments account for between 6.3% in Oman and 61.8% in Egypt; and development assistance generally accounts for between 0% and 1%.

3.2. Pharmaceutical market size and expenditure

Table 4 provides an overview of pharmaceutical market size in terms of total spending and as a proportion of GDP and of health expenditure in the eleven study countries. It also summarises the relative importance of patented vs generic segments, and Rx vs OTC segments.

Table 4: Pharmaceutical expenditure and relation to health expenditure, 2016

	Pharma-ceutical spending (% of GDP)	Pharma-ceutical spending (% of health spending)	Pharma-ceutical spending, (US$ bn)	Patented pharma-ceutical spending (% total spending)	Generic pharmaceutical spending (% total spending)	Rx pharma-ceutical spending (% total spending)	OTC pharma-ceutical spending (% total spending)
Algeria	2.31	31.2	3.699	52.0	32.5	84.6	15.4
Bahrain	1.20	20.0	0.393	57.7	31.7	89.8	10.6
Egypt	1.31	25.9	3.538	50.3	32.2	82.5	17.5
Jordan	2.85	33.8	1.034	34.5	48.3	82.9	17.2
Kuwait	0.93	18.1	1.018	63.8	21.1	84.9	15.1
Lebanon	3.47	49.3	1.726	49.5	30.8	80.4	19.6
Morocco	1.35	23.8	1.401	41.2	29.7	70.9	29.1
Oman	0.90	21.7	0.668	48.8	39.8	88.6	11.4
Qatar	0.36	11.0	0.554	68.6	21.2	89.8	10.2
Saudi Arabia	1.16	21.6	7.443	54.5	32.5	87.0	13.0
UAE	0.67	16.3	2.617	67.2	18.4	85.6	14.4

Source: LSE from market research sources.

Generally, across the study countries, OTC pharmaceutical sales comprise a significantly smaller share of total sales, compared with prescription pharmaceutical sales.

Furthermore, patented pharmaceuticals sales comprise a greater proportion of total sales than generic pharmaceutical sales.

Pharmaceutical spending ranges between 0.36% and 3.47% of GDP and between 11% and 49.3% of health expenditure in the study countries. Pharmaceutical spending as a proportion of health expenditure is highest in Lebanon (49.3%), Jordan (33.8%) and Algeria (31.2%). Likewise, pharmaceutical spending as a proportion of GDP is highest in the same three countries: Lebanon (3.47%), Jordan (2.85%), and Algeria (2.31%). Of the eleven study countries, pharmaceutical spending is lowest as a proportion of GDP or health expenditure in Qatar (0.36% and 11.0%, respectively), UAE (0.67% and 16.3%, respectively), and Kuwait (0.93% and 18.1%, respectively).

4. Pharmaceutical pricing policies

4.1. Pricing policies for pharmaceuticals

4.1.1. Pricing policies for in-patent pharmaceuticals

Across the study countries prices of in-patent pharmaceuticals are set based on a variety of criteria summarised in **Table 5**. The dominant method of pricing is ERP, which is used across all study countries, but additional criteria may apply, for example, the product price in the country of origin, the prices in the GCC region, the prices in official reference sources, such as the British National Formulary (BNF), when available, and the prices of pharmaceuticals in the same therapeutic category (Abuelkhair et al., 2012; Alrasheedy et al., 2017; Al Abbasi and Al Jalahma, 2017; Kalo et al., 2015; Khan et al., 2016; BMI 2016e, 2017i; Qarain et al., 2009; WHO and HAI, 2011; World Health Organization, 2011c, 2011d).

Pricing of pharmaceuticals in the region often combines ERP and IRP to derive the price of similar products in the same therapeutic class. IRP is usually used as a benchmark to keep prices of similar products aligned. For example, in Bahrain, Oman, Saudi Arabia, and the UAE, the prices of similar products available in the market should be proportionate to the price derived by ERP. Interestingly, according to new Ministerial decrees, a few countries (Bahrain, Jordan, and Saudi Arabia) are now considering the therapeutic significance of new pharmaceuticals and (may) require pharmacoeconomic studies during price setting, while others (Algeria, Lebanon, Morocco) are explicitly considering comparative clinical benefit assessment and may require pharmacoeconomic studies as criteria to inform pricing decisions, although the intensity and methodological robustness, particularly as concerns pharmacoeconomic evidence, varies. In some of the study countries, additional (importer) margins are applied to the final price of pharmaceuticals. In Egypt and Morocco,

an additional importer margin is applied to the price while in Oman and Bahrain retail prices are based on fixed profit margins, which are the allowable profit of the distributor and the retailer (Primary Evidence: Egypt and Morocco, 2018; BMI, 2017i; Al Abbasi and Al Jalahma, 2017).

In 2014, GCC countries implemented a unified pricing policy, setting a single price within the region to control pharmaceutical prices and contain pharmaceutical spending. Under unified pricing, different Cost and Insurance Freight (CIF) prices are provided to different GCC counties. Representatives of all the GCC countries meet in Saudi Arabia, to examine the different CIF prices in the GCC basket and decide on a unified CIF price (Primary Evidence). In a first stage, the unified pricing policy was implemented by government-run facilities, which were directly reflected on private pharmacies across the region (UAE Government News, 2013).

Individual country pricing policies are subject to some variability and are briefly outlined below. The salient features of ERP systems across the region are presented in the next section.

In ***Egypt***, pricing of in-patent pharmaceuticals precedes the marketing authorisation process (Primary Evidence: Egypt, 2018). In 2012, Egypt changed the way prices were set for in-patent pharmaceuticals from cost-plus pricing (CPP) to ERP (Kalo et al., 2015; Mohamed, 2014). If a new pharmaceutical product is available in fewer than five countries in its basket, the pricing committee in the MoH will request from the pharmacoeconomic unit to perform a pharmacoeconomic 'rapid review'. This review takes place in order to select the best comparison for this product and price the product according to its economic value and competitiveness (Primary Evidence: Egypt, 2018). Cost-effectiveness pricing is used in the reimbursement process or in specific circumstances. For example, if an expensive drug is priced at a low price and manufacturers appeal, the pricing committee of the MoH might request a pharmacoeconomic study (Primary Evidence: Egypt, 2018). Clinical data for the study are based on international studies whereas economic data are based on Egyptian (unit) costs. In the Egyptian pricing system, there are still provisions for price increases. A manufacturer could present the product's cost sheet, which includes the CIF price, the profit margin and the customs and tariffs, and subsequently request a price to be set on the basis of the reported cost. Each manufacturer is allowed to request a price increase for not more than 5% of the firm's registered portfolio yearly, but the MoH still retains the right to accept or refuse any request for price increase (Mohamed, 2014). An additional 6% importer margin is applied to the price of all pharmaceuticals. In Egypt, cost-effectiveness pricing is only used in the reimbursement process or in specific cases. For example, if an expensive drug received a low price, the manufacturers can appeal and

request from the Pricing Committee to conduct a pharmacoeconomic study (Primary Evidence: Egypt, 2018).

In the ***United Arab Emirates (UAE)*** imported drugs under patent are priced using ERP (Mohamed, 2014). The prices of in-patent pharmaceuticals are set according to the lowest price of the following: (i) ex-factory price in the country of origin; (ii) import price proposed by the company including the freight and insurance costs until the delivery at the country port; (iii) the median of the approved CIF price of the product in the list of the reference countries. In addition, the following criteria should also be taken into account when setting the prices of in-patent pharmaceuticals: i) therapeutic significance of drugs; ii) prices of similarly registered or therapeutically equivalent or alternative drugs; iii) pharmaco-economic studies; iv) factory price, wholesale price and public price in the country of origin in USD; v) price proposed by the manufacturer in USD or AED including CIF inside the ports of the country; vi) Export price to reference countries; and vii) Guidance on the price of countries that product is marketed. In the UAE, distributor profit margin is 15% of CIF and pharmacy profit margin is specified as per the fixed (CIF) price: i) 0 – 250 AED: 28% of pharmacy price; ii) 250 – 500 AED; 24% of pharmacy price; and iii) More than 500 AED: 20% of pharmacy price (UAE Ministry of Health and Prevention, 2018). Pharmaceuticals and medical devices are zero rated after application of the VAT in the UAE as of 1 January 2018.

Similarly, prices of in-patent pharmaceuticals in ***Oman*** are priced based on the price of the drug in country of origin and GCC countries as well as the price of other pharmaceuticals in the same therapeutic group and the price of pharmaceutical in official references such as the British National Formulary (World Health Organization 2011c, 2011d). Retail prices are based on the CIF price and based on a profit margin of 45%, which is 19% to the wholesaler or the distributor and 26% to the retailer (Alkhuzaee et al., 2016; Awaisu et al., 2014; BMI, 2017e; WHO, 2011d). The MoH enforces this profit margin cap as a part of price unification across the GCC region (BMI, 2017e).

In ***Jordan***, prices of pharmaceuticals have been set using ERP since 2003, upon registration of the product by the Jordan Food and Drug Administration (JFDA) (Primary Evidence: Jordan, 2018; Hammad, 2016; Kalo et al., 2015). The pharmaceutical price should be the lowest of the following benchmarks: the price in the country of origin, the median price of the reference basket, the export price set by the manufacturer and the public price in Saudi Arabia. If the drug is only available in its country of origin, the price is based on drug prices having close chemical composition or therapeutic effect. In addition, if the pharmaceutical is not registered in Saudi Arabia, the Jordanian price will

be reviewed once it is registered in Saudi Arabia. Jordanian authorities should be informed about the CIF export price to Saudi Arabia within four months from the date of pricing in Saudi Arabia (Primary Evidence: Jordan, 2018; El-Dahiyat and Curley, 2017; Hammad, 2016; Kaló et al., 2015; Kanavos et al., 2018; Qarain et al., 2009). Since 2012, when a new pharmaceutical is registered in the JFDA and it is only available in the country of origin and in three of the preselected referenced countries, evidence on the cost-effectiveness of the pharmaceutical is required to inform pricing decisions. If the new pharmaceutical demonstrates additional clinical and therapeutic benefits, then a premium price can be fixed over any of the aforementioned prices (Hammad, 2016). However, according to evidence in the literature, there is no official guidance on how economic evidence could inform pricing decisions, resulting in minimal influence on the final price setting (Hammad, 2016). Wholesale and retail mark-ups are standard for all pharmaceuticals in Jordan. Wholesalers receive 15% on the cost at port of entry plus 4% for expenses, while a pharmacy receives 20% on the wholesale price plus 6% expenses. For imported medicines, other charges include an insurance fee (1%), bank fee (1%), transport and clearance fee (1.5%), added fee (0.2%), VAT (4%), and for some medicines, excluding antibiotics, an import fee of up to 5% is charged depending on the country of origin (World Health Organization (2007a).

Pricing of pharmaceuticals in ***Bahrain*** are also set upon registration of the product, considering the price of the pharmaceutical in the country of origin, CIF prices in GCC region, the therapeutic significance of the drug and if available pharmacoeconomic studies, drug price in official pricing references and prices of similar drugs in Bahrain (Al Abbasi and Al Jalahma, 2017). Higher prices for pharmaceuticals can be adopted in Bahrain when the pharmaceutical contains additional substances, which can increase the drug efficacy or add therapeutic value to the product or when a pharmaceutical has additional technical advantage that can increase the drug efficacy or adds therapeutic value to the drug (Al Abbasi and Al Jalahma, 2017). Maximum profit margins for distributors and retailers combined should not exceed 45% of CIF prices (Al Abbasi and Al Jalahma, 2017). In case of registering the innovator drug after the registration of the generic drug, the innovator drug will be priced according to the lowest price resulting from applying the above mechanisms, with the condition that it does not exceed the price of the generic registered first. In such cases, the price of the innovator may be given a lower price than the generic registered first. While in the case of registering the generic drug before the registration of the innovator drug, the generic drug will be dealt with as the innovator and priced accordingly (Al Abbasi and Al Jalahma, 2017).

In ***Saudi Arabia***, the Saudi Food and Drug Authority (SFDA) is setting prices for pharmaceuticals using the following criteria: (i) ex-factory and wholesale price in the

country of origin; (ii) public prices in the country of origin and other countries where the product is marketed; (iv) CIF price to Saudi Arabia in the country of origin currency;(v) CIF prices to countries in which the product is marketed ; and if available (vi) the price in official pricing references; (vii) therapeutic significance of the product; (viii) pharmacoeconomic studies of the product; (ix) prices of similar medicines that are registered in Saudi; and (x) the proposed price by the manufacturer (Alrasheedy et al., 2017; Kalo et al., 2015; Khan et al. ,2016; BMI, 2016e, 2017i; Qarain et al., 2009). Whereas, prices of in-patent pharmaceuticals with similar products in the market are based on the aforementioned pricing criteria, prices of similar products available in Saudi Arabia, the benefits to risks ratio, the cost of therapeutic regimen and the cost of daily therapeutic dose (Qarain et al., 2009). Saudi Arabia also reserves the right to increase a product price by 5% to 30% more than the original product depending on the country of origin (Kanavos et al., 2018). In a situation comparable to Jordan, where economic evaluations are used in certain cases, in Saudi Arabia the use of evidence of health-related economic evaluations is not mandatory when a new pharmaceutical is licensed and it is used only on an ad-hoc basis. Evidence from the systematic literature review has shown that economic evaluations tend to be heterogeneous and only assess an intervention after its diffusion into the market (Al-Aqeel, 2012; Al Hussein et al., 2009; Qarain et al., 2009). A more systematic approach to the use of economic evidence the existence of guidance on the collection and evaluation of evidence, would improve the confidence in the findings of economic evaluations and their ability to inform decisions concerning allocation of health care resources (Al-Aqeel, 2012; Al Hussein et al., 2009; Qarain et al., 2009). Pharmaceuticals and Medical Devices are zero rated after application of the VAT in Saudi Arabia as of 1 January 2018.

Qatar has set prices of pharmaceuticals based on the unified GCC price since 2014, which references CIF prices across the GCC region (Primary Evidence: Qatar, 2018). Only in-patent pharmaceuticals are included under ERP regulation (Primary Evidence: Qatar, 2018). In addition, in Qatar, a maximum profit of 40% is added to the unified CIF plus 4% expenses. The 40% profit is of 15% for supplier and 25% for retailer (Primary Evidence: Qatar, 2018; BMI, 2017i).

Algeria, Lebanon, Kuwait and Morocco use ERP (Primary Evidence: Algeria, Kuwait, Lebanon, Morocco, 2018; Awaisu et al., 2014; BMI, 2017d; Kalo, et al.,2015). In Morocco, in addition to the price derived from ERP for new pharmaceuticals, a 10% importer margin is applied plus the minimum prices of Active Pharmaceutical Ingredients (API), while the pharmacists' margin is set at 30% of the pharmaceutical product's price (Primary Evidence: Morocco, 2018). In Lebanon, a 7.5% is added to the price of imported pharmaceuticals as freight expenses and 11.5% for clearance duties and other expenses

if the price is Free on Board (FOB). In case the price is CIF then only 11.5% for clearance duties and other expenses is added.

Table 5: Pricing criteria for price setting of in-patent pharmaceuticals in the MENA Region, 2018[1]

	Price in country of origin	Price of similar pharmaceuti-cals on the market – IRP[5]	Prices found in official references or publications[2]	Therapeutic Significance	Pharmaco-economic studies/ Cost-Effectiveness Evidence[3]	ERP	Price in Saudi Arabia	Proposed price by the manufacturer
Algeria	-	-	-	-	-	✓	-	-
Bahrain	✓	✓	✓	✓	✓	✓	-	-
Egypt	-	-	-	-	-[6]	✓	-	-
Jordan	✓	(✓)[4]	-	-	✓	✓	✓	✓
Kuwait	-	-	-	-	-	✓	-	-
Lebanon	✓	-	-	-	-	✓	-	-
Morocco	-	-	-	-	-	✓	-	-
Oman	✓	✓	✓	-	-	✓	-	-
Qatar	-	-	-	-	-	✓	-	-
Saudi Arabia	✓	-	✓	✓	✓	✓	-	✓
UAE	✓	-	✓	-	-	✓	-	✓

Notes: [1] Combining primary and secondary evidence, the latter not necessarily from 2018.

[2] Refers to prices found in official publications and in addition to those from reference countries. For example, the British National Formulary (BNF) is such a source and constitutes an additional criterion for pricing.

[3] Pharmacoeconomic analysis is not an explicit requirement for the countries shown on this column and, in most cases, it is used in selected conditions only.

[4] If the pharmaceutical is only available in the country of origin.

[5] Internal reference pricing, which practically signals that reimbursed prices subscribe to a ceiling imposed by the competent authority.

[6] Although there is no evidence that this is used in practice in Egypt, there is some infrastructure/expertise on the subject at MoH level.

Key: '✓' = Yes/used.

'-' = No evidence that this is used in practice.

Sources: The authors based on findings of primary and secondary evidence.

4.1.2. Pricing policies for off-patent pharmaceuticals

Evidence on the pricing of off-patent pharmaceuticals in the literature is very scarce. In ***Saudi Arabia***, prices of off-patent products with generic competitors are lowered by 20% to 30% of their original registered price; consequently, the off-patent originator price stands at 70-80% of the original originator price. This new price is applied to the originator one year after the generic product is registered (Primary Evidence: Saudi Arabia, 2018; Alkhuzaee et al., 2016; Alrasheedy et al., 2017; Kanavos et al., 2018; Khan et al., 2016). In ***Jordan***, off-patent pharmaceuticals are priced based on the same pricing criteria for in-patent pharmaceuticals (Primary Evidence: Jordan, 2018; BMI, 2017c, 2016c). Similarly, in ***Algeria*** and ***Qatar***, off-patent pharmaceuticals are priced using ERP (Primary Evidence: Algeria and Qatar, 2018). In Algeria, however, ERP is used in conjunction with a 10% price cut applied to off-patent pharmaceuticals every five years. In ***Morocco***, the price of an off-patent pharmaceutical is set as a fixed percentage below the originator's price (Primary Evidence: Morocco, 2018). Off-patent pharmaceuticals in ***Lebanon*** are subject to internal price referencing (IRP) (Primary Evidence: Lebanon, 2018). In ***Kuwait***, prices of off-patent pharmaceuticals are set through price capping, where the price for the off-patent product is set at 20% lower than the originator's original price before the loss of exclusivity (Primary Evidence: Kuwait, 2018).

4.1.3. Pricing policies for generic pharmaceuticals

Prices of generics in the MENA region are usually set as a fixed percentage below the originator price (price capping), with prices varying from first generics to the following ones entering the market (managed competition). **Table 6** summarises the pricing policies followed in price setting of generic pharmaceuticals in the study countries.

Prices of imported generics in ***Egypt***, are set at a fixed percentage below the originator's price. Prices of the first five generics entering the market are set 35% below the originator's price while 40% below applies for follow-on generics (Primary Evidence: Egypt, 2018; Mohamed, 2014; Mohamed and Kreling, 2016; Wanis, 2015). High-technology generic products are discounted from the innovator price by 30% for imported products from a reference country. The price must not exceed the selling price in its country of origin or any country where it is currently on the market. Generic products that are imported from non-reference countries are discounted at 35%. This price may also not be listed higher than the selling price in the country-of-origin (Kanavos et al., 2018). Prices of locally manufactured generics are set 60 to 75% below the price of the originator for

the first four generics and for the following generics a 10% reduction is applied to the latest preceding generic (Qarain et al., 2009).

In the ***UAE***, the first imported generic shall be specified by adopting the lesser of the following prices: i) calculating 60% of CIF approved for the innovator before deduction; ii) ex-factory price in the country of origin (COO) with an addition of 20%; iii) CIF price proposed by the company; and iv) the median CIF price approved for the drug in the list of reference countries. For the second and third imported generics, the above hold, except that for the second one we calculate 50% of CIF approved for the innovator before deduction and for the third one we calculate 40% of CIF (UAE Ministry of Health and Prevention, 2018). For *wholly* locally manufactured generics, the pricing is a price capping formula (70% of innovated drug with a reduction of 30% in the price of innovated drug) regardless of its chronological order or the number of other products. The pricing of the *partially* locally manufactured generic (part of the manufacturing occurred locally) follow the same pricing strategies of the points 1-3 above.

In ***Kuwait***, generics are priced based on an overall price capping system, infused with managed competition on the basis of sequence of entry. First, after loss of exclusivity, the originator price declines by 20%; then, the first generic to the market receives a price 15% lower than the reduced price of the off-patent originator pharmaceutical; the second to the fifth are reduced by a further 10%, and the sixth to the eight a further 5%. After the eight generic the price remains fixed, unless a lower price is submitted by the manufacturer (Primary Evidence: Kuwait, 2018; Ball et al., 2005).

In ***Morocco***, the price of any generic drug, locally manufactured or imported, is established on the basis of the maximum reference price (MRP). This is calculated from the minimum rate of reduction of the initial manufacturer's selling price (MSP) of introduction of the original medicine concerned. Where the originator is not marketed in Morocco, the MRP shall be calculated on the basis of the minimum reduction rate of the theoretical MSP of the originator obtained by applying the comparison of the MSP fixed or approved by the competent authorities in the following countries: Saudi Arabia, Belgium, Spain, France, Turkey, Portugal and in the country of origin (Primary Evidence: Morocco, 2018). The first nine generics are priced 50% cheaper than the off-patent originator pharmaceutical, given that retail price in Morocco is lower or equal to 250 Moroccan dirhams. If the price of the off-patent originator is higher, the first nine generics are priced up to 50% less than the price of the originator. All generics that follow after that are priced 20% lower than the first nine generics (BMI, 2017d, 2016d; Kanavos et al., 2018). If the generic product already exists in the market, the generic price decreases by 15% compared to the originator for the second generic to enter the market, 30% for the third, and 35% for the fourth. If the first generic does not exist in the market, it is priced by the

lowest price of the originator in the reference countries. The first generic is not discounted; the second follows the same regulations as above: decreased by 15% for the second entrant, 30% for the third, and 35% for the fourth (Primary Evidence: Morocco, 2018; Kanavos et al., 2018).

In ***Jordan***, imported generics are priced based on the same criteria for the pricing of in-patent pharmaceuticals (Primary Evidence: Jordan, 2018; El-Dahiyat and Curley, 2017). Where the drug has a registered generic equivalent, the price is determined as the lowest price resulting from the application of different methods, including (a) The export price to the Saudi Market, and if it is not registered there, its pricing shall be reviewed upon its registration and the agent is committed to provide JFDA with the price within a period not exceeding four months; (b) Provided that the requested price does not exceed 80% of the price of the originator drug when first registered and priced or upon re-pricing it or 80% of its current price whichever is less (Primary Evidence: Jordan, 2018). Locally manufactured generics are priced at 80% of the originator price or 70% of the originator's price in case of contract manufacturing (Primary Evidence: Jordan, 2018; BMI, 2017, 2016; El-Dahiyat and Curley, 2017; Kanavos et al., 2018; Qarain et al., 2009).

In ***Saudi Arabia***, the price of imported generics is set following the lowest price in one of the following benchmarks: (i) the common pricing criteria described earlier in this report (section 4.1.2) and (ii) the therapeutic significance of the product. In addition, the price should not exceed the lowest price of similar products in Saudi Arabia (Qarain et al., 2009). Imported generics with locally manufactured generic competitors, first imported generic will be priced 10% below the price of the locally manufactured generics and subsequent generics would receive 10% less than latest preceding generic (Alkhuzaee et al., 2016; Alrasheedy et al., 2017; Khan et al., 2016; Qarain et al., 2009). Generics that have been manufactured and are available in the US or are registered in Europe, the Middle East and Africa, are priced 30% below the originator if the generic first entered the market and 10% below the price of the first generic for following generics (Alkhuzaee et al., 2016; Alrasheedy et al., 2017; Khan et al., 2016; Qarain et al., 2009). Locally manufactured generics, must be priced 65% less than the originator (Kanavos et al., 2018). The first generic entrant is marked 15% less than the updated price of the off-patent originator (which is at minus 20% to 30%), the second generic is then marked down by an additional 10%. Each generic registered after the second will be discounted by 10% until the fourth generic. The price of the fourth generic becomes the ceiling price for the following generics to enter the market and any additional generic to enter the market after the fourth, takes the price of the fourth generic (Kanavos et al, 2018). If the generic is registered by a local manufacturer and the originator is not available in the Saudi market, there is a list of

reference countries that will be used to price the product (Kanavos et al., 2018). However, which countries would be referenced is not clear (Kanavos et al., 2018).

In ***Bahrain***, the price of generics is calculated based on lowest price derived by one of the following criteria: first, the computed price form the ex-factory price in the country of origin (COO) plus the cost of insurance and shipping; second, the lowest CIF prices in the reference basket of GCC regions and other countries; third, the prices of drugs in the same therapeutic category and/or with the same therapeutic effect, and, finally, the price on the basis of its registration order, where the price of the first generic is 15% below the price of the originator drug (already declining by 20% at patent expiry), the price of the second generic is 10% below the price of the first generic drug, the price of the third generic is 10% below the price of the second generic, up to the fourth generic drugs; the price of the 5th generic drug and anyone above that is lower than or equal to the price of the 4th generic drug (Al Abbasi and Al Jalahma, 2017; Primary data collection: Bahrain, 2018). Thus, the pricing formula of Bahrain can be described as "price capping with managed competition" (see also Table 6).

In ***Oman***, generics are priced according to ERP, where the price of the drug in the country of origin, in GCC region and the number of similar drugs registered in the country, should be taken into consideration (WHO, 2011c, 2011d).

In ***Qatar***, the pricing of generics is based on the CIF price that Qatar receives. Qatar also employs profit controls to price generics (Primary Evidence: Qatar, 2018). The price of generics cannot be higher than the sale price in the country of origin (Primary Evidence: Qatar, 2018).

In ***Algeria***, cost-plus pricing is used to price locally manufactured generics. This policy allows 20% profit margin calculated based on direct and indirect costs (Primary Evidence: Algeria, 2018). ERP is used for imported generics, where, the price is benchmarked with the price of the imported generic of the same manufacturer in the basket countries, if available. In addition, locally manufactured generics should be priced 20% below the originator and imported generics should be priced 30% below compared to the originator price, both before and after loss of exclusivity (Primary Evidence: Algeria, 2018).

In ***Lebanon***, generics similarly to off-patent pharmaceuticals are priced based on internal reference pricing (IRP) (Primary Evidence: Lebanon, 2018).

Table 6: Price setting of generic pharmaceuticals in the MENA Region, 2018[1]

	Fixed percentage below the originator's price (Price capping)	ERP	Other Criteria
Algeria	✓ For locally manufactured generics	✓ Imported generics	✓ Locally-manufactured generics: Cost-plus pricing
Bahrain[2]	✓ 1st generic at [P of originator - 20%]-15%; 2nd generic: P of 1st generic – 10% 3rd generic: P of 2nd generic – 10% 4th generic: P of 3rd generic – 10% Following generics: ≤ P of 4th generic	✓	✓ There are elements of dynamic competition (stepwise decline of 2nd, 3rd, 4th and 5th generic) Lowest price in one of the following: (i) the computed price from the ex-factory price in the country of origin plus the cost of insurance and shipping; (ii), the lowest CIF prices in the reference basket of GCC regions and other countries; (iii), the prices of drugs in the same therapeutic category and/or with the same therapeutic effect, and; (iv), the price on the basis of its registration order
Egypt	✓	✓ Imported generics	✓ Locally-manufactured generics: cost-plus pricing
Jordan	✓	✓ (for imported generics)	✓ Imported generics: priced based on the criteria for the pricing of in-patent pharmaceuticals Locally manufactured generics: maximum price at 80% of the originator price
Kuwait[2]	✓ 1st generic at [P of originator – 20%] - 15%; 2nd to 5th 10% reduction sequentially; 6th to 8th 5% reduction sequentially; 8th generic onwards fixed price, unless companies submit lower price	×	×
Lebanon	×	×	✓ Internal reference pricing
Morocco	✓	✓	✓ Based on the maximum reference price (MRP)
Oman	-	✓ COO and GHC countries	✓ Number of similar products registered in the country
Qatar	'Profit controls'	×	✓

			Based on the CIF price that Qatar receives, or through profit control. The price of generics cannot be higher than the sale price in the country of origin
Saudi Arabia[2]	✓ (locally produced generics)	×	✓ Imported generics: the lowest price in: (i) the common pricing criteria (ii) the therapeutic significance of the product Locally produced generics: price capping with managed competition (stepwise price reduction for first and subsequent generics)
UAE	✓ (for wholly locally manufactured generics)	×	Imported generics (including partially locally manufactured ones): Lowest price in one of the following: i) Calculating 60%, 50%, or 40% (for 1st, 2nd, and 3rd to market, respectively) of CIF approved for the innovator before reduction; ii) Ex-factory price in the country of origin with an addition of 20%; iii) CIF price proposed by the company; and iv) Median CIF price approved for the drug in the list of reference countries. Locally manufactured generics: price capping at 70% of the off-patent originator (which may have lost a further 30% upon loss of exclusivity)

Note: [1] Based on the results of primary data collection, whereas secondary sources, where used, reflect earlier years. There may be discrepancies in the application of some of the rules outlined in the table.

[2] Following loss of exclusivity, the off-patent originator's price declines by 20%. In Saudi Arabia the reduction to the originator price is in the region of 20-30%.

Key: '✓' = yes / used
'×' = no / not used
'-' = no evidence

Sources: The authors based on findings of primary and secondary evidence.

4.1.4. Pricing policies for locally manufactured pharmaceuticals

There are differences in the criteria in which locally manufactured pharmaceutical products are priced in the study countries, compared with imported pharmaceuticals (both brand and generic). In ***Morocco***, prices of locally manufactured pharmaceuticals are not set based on ERP (Primary Evidence: Morocco, 2018). The retail price of locally manufactured pharmaceuticals is based on the manufacturer's price, the pharmacy margin, which is 30%, the distributor margins, which is 10% and a reduced rate of VAT of 7% (BMI, 2017d, 2016f). In ***Lebanon***, locally manufactured drugs are priced according to the cost of production, the price of similar drugs, the cost and profit index and the classification of the pharmaceutical manufacturing company. In addition, the following are taken into consideration: (i) the price in US$ of imported raw materials, (ii) some indirect costs such as salaries, packing materials, charges, drugs marketing, and (iii) other miscellaneous costs. A 10% and 30% are added to the price as distributor profit and pharmacist benefit respectively. (Primary Evidence: Lebanon, 2018). In ***Saudi Arabia***, the following criteria are followed to set the prices of locally manufactured drugs. First, products manufactured

under license and under patent, which are registered and priced for the company which is the licensor, are given the same price of the licensor. Second, products manufactured under license and still under patent, which are introduced for the first time through a local manufacturer, will be priced according to the common pricing criteria as explained above, assuming the price is given to the licensor company and then be given to the local manufacturer at the same price. Third, products manufactured under license and still under patent, which is produced locally under the name given by a local manufacturer are priced 10% less than the accredited price for the licensor company (Qarain et al., 2009).

In ***Egypt***, locally manufactured pharmaceuticals are priced based on 65% and 60% of originator price for the first and last five applications respectively. High margins are applied for pharmacists and distributers (Primary Evidence: Egypt, 2018; Kanavos et al., 2018).

In the ***UAE***, completely locally manufactured generics are priced at 70% of the innovator, without considering the time order and number of products. Partially locally manufactured generics (part of manufacturing process or contract manufacturing) are priced at 60% (first generic), 50% (second generic) and 40% (third generic) of the innovator (UAE Ministry of Health and Prevention, 2018).

4.1.5. Pricing policies for multinational manufacturers

In the ***UAE***, if the owner company of the innovator product wishes to manufacture one of its products locally or transfer one of its manufacturing phases in one of the local factories, the same price approved for the innovator drug is offered and a 5-year protection period of reviewing of prices is given from the date of contract commencement. If the owner company wishes to provide one of the local factories with the license for a second brand, this second product is offered at the same price as the innovator product during a protected patent period (UAE Ministry of Health and Prevention, 2018).

4.2. The role and key features of ERP

4.2.1. Price calculation

In all study countries the reference price is calculated based on the lowest price in the basket, with the exception of Jordan and the UAE, which use the median price of the basket, and Kuwait, which uses the average price (Primary Evidence: all countries, 2018; Abuelkhair et al., 2012; Al Abbasi and Al Jalahma, 2017; BMI, 2017c, 2016c, 2017g, 2017i; El-Dahiyat and Curley, 2017; Hammad, 2016; Kalo et al., 2015; Khan et al., 2016; Mohamed, 2014; Qarain et al., 2009; WHO, 2011c, 2011d; WHO and HAI, 2011). In Morocco the average price of the basket is considered for existing products contrary to the

lowest price which is considered for newly launched products (Primary Evidence: Morocco, 2018).

4.2.2. Reference basket

Reference baskets tend to vary in the MENA region from small baskets such as Kuwait, Oman, and Qatar, which reference the GCC region, to very large baskets such as Egypt and Saudi Arabia. Saudi Arabia recently increased its basket from 30 to 40 countries (Kanavos et al., 2018). The reference list now includes low-middle income countries such as Bosnia and Herzegovina, Brazil, the Czech Republic, Malaysia, Mexico, Poland, South Africa and Tunisia. These countries were added to continuously drive prices of pharmaceuticals down (Kanavos et al., 2018). **Table 7** summarises the salient features of ERP systems across the study countries.

4.2.3. Prices used to inform ERP

The type of comparator prices used to inform the pricing of pharmaceuticals are presented in **Table 7** and include ex-factory, wholesale, retail or CIF prices in some combination.

4.2.4. Sources of information for pricing decisions

The implementation of ERP requires access to price information. In Algeria, Egypt, Jordan, Lebanon, Morocco, Oman, Qatar, and the UAE, pharmaceutical manufacturers are responsible for providing pricing information to the competent authority (Primary Evidence: all countries, 2018; WHO and HAI, 2011). In Qatar, confidential pricing information on GCC CIF prices is also used (Primary Evidence: Qatar, 2018). In Jordan, Egypt, Algeria, Morocco and UAE, public websites are also used as sources for identification and validation of ERP prices (Primary Evidence: all countries, 2018; WHO and HAI, 2011). Kuwait uses a combination of manufacturer information, and private and public sources (Primary Evidence: Kuwait, 2018).

4.2.5. Price revisions

In ***Egypt***, prices are revised every five years. However, according to evidence this is not followed in practice (Primary Evidence: Egypt, 2018; Kalo et al., 2015; Mohamed, 2014; Wanis, 2015). Price revisions are also taking place when the currency exchange fluctuations of average 15% goes up or down in a year and when the manufacturer might request price revisions for their products not exceeding 5% of its products per year (Wanis, 2015). In ***Jordan***, prices are revised every two years upon drug's registration and again upon renewal. At re-registration time of each product, which occurs every five years of

the product lifecycle, products are re-priced according to specific criteria. Additionally, prices are revised when exchange rate fluctuations of the drug prices or changes in currency exchange rates are taking place in the country of origin and in the reference basket. Finally, prices are revised four months after the price reduction of the drug in a reference country (Primary Evidence: Jordan, 2018; BMI, 2017; Kanavos et al., 2018). In ***Bahrain***, price revision can take place during the registration period of a drug (typically lasting for 5 years) and during the registration renewal. In the registration period, price revisions are performed if there is a price reduction in the country of origin and/or the price of in-patent product; if the drug has been registered in a lower price in another GCC country; if there is a change in the manufacturing site, and; if the manufacturer requests such a revision (Al Abbasi and Al Jalahma, NHRA, 2017). In ***Saudi Arabia***, the proposed price is revised and/or approved by the Registration Committee for drug companies, manufacturers and their products, which should approve fair prices calculated according to the pricing guidelines, 'The Rules for Pharmaceutical Products Pricing', as outlined by the SFDA (Primary Evidence: Saudi Arabia, 2018; Khan et al., 2016). Price revisions take place at the time of renewal of product registration every 5 years (Khan et al., 2016). In ***Algeria***, price revisions take place every five years, or when the price changes in the country of origin or in key basket counties. Five-year revisions are not applicable for locally manufactured pharmaceuticals. However, revisions can occur on molecular basis for instances when prices of originator might drop considerably (Primary Evidence: Algeria, 2018). In ***Morocco***, prices of imported in-patent pharmaceuticals and generics are revised when the exchange rate varies by more than 10%. Price revisions are also the result of the annual referencing of the benchmarked basket (BMI, 2017d, 2016d). Pricing is updated also when an originator loses its market exclusivity or there is a change in the pharmaceutical formula or packaging (Primary Evidence: Morocco, 2018). Prices in Morocco are revised during the Marketing Authorisation renewal, every five years and when price changes in key basket countries occur (Primary Evidence: Morocco, 2018). There are two kind of price reviews in the ***UAE***, periodic and exceptional. In terms of periodic reviews, all innovative and generic drug prices are revised every five years, along with the renewal of product registration. An exceptional review is taking place in the following cases: i) In case of expiry of an innovator's patent, 20% of the price is reduced and, upon its revision, the price of its generics should also be reduced by 20%; ii) In case of any minor changes on the product; iii) Upon request of health authorities (REF: new UAE guidelines). In ***Kuwait and Qatar***, price revisions only occur when the price changes in key basket countries (Primary Evidence: Kuwait and Qatar, 2018).

4.2.6. Price adjustments

Price adjustments are implemented to account for exchange rate fluctuations. In ***Lebanon, Morocco, Bahrain*** **and** ***Jordan*** price adjustments are taking place (Al Abbasi and Al Jalahma, 2017; Ammar, 2009; BMI, 2017, 2016d). In Lebanon, prices are set according to a Ministerial Decision, which provides an updating mechanism for pharmaceutical prices, issuing a price index taking into account the moving average (Primary Evidence: all countries, 2018; Ammar, 2009). In ***Bahrain*** **and** ***Qatar***, all CIF prices are set in one currency (US$) to prevent currency fluctuations (Primary Evidence: Bahrain and Qatar, 2018; Al Abbasi and Al Jalahma, 2017). The same applies in ***Jordan***, where only a single currency is considered, either the currency of country of origin or US dollars or Euros (Primary Evidence: Jordan, 2018). In ***Kuwait***, a fixed exchange rate (the average over the past six months) is set by the Ministry (Primary Evidence: Kuwait, 2018). In the ***UAE*** and ***Algeria***, no price adjustments are applied to mitigate exchange rate fluctuations (Primary Evidence: UAE, Algeria, 2018). In ***Egypt***, the pricing method does not allow for price increases to compensate for inflation, though price revisions are taking place when there are currency exchange fluctuations. Monthly exchange rates set as per central bank rates are used when translating prices from foreign currencies (Primary Evidence: Egypt, 2018; BMI, 2017b, 2016b; Mohamed, 2014; Wanis, 2015; Qarain et al., 2009). The recent depreciation of the Egyptian pound has resulted in shortages of a number of pharmaceutical products in Egypt, including locally manufactured generics.

Table 7: Salient features of ERP in the MENA Region

	Price Calculation	Number of Basket countries	Countries in the Basket	Price source	Sources of information for pricing decisions	Price Revisions	Price adjustments
Algeria[1]	Lowest price	9[7]	Belgium, France, Greece, Morocco, Spain, Tunisia, Turkey, UK; plus Country of origin (COO)	Ex-factory and retail prices in basket countries	Manufacturers and public information sources (e.g. websites)	Every 5 years and when the price changes in the country of origin or in key basket counties	×
Bahrain	Lowest price	>6[7,8]	Kuwait, Oman, Qatar, Saudi Arabia, and the UAE; plus COO; plus other countries not specified in pricing guideline	Ex-factory and CIF price in basket countries	-	Can take place at re-registration, but also anytime w/in the 5 year registration period if: (i) there is a price reduction in the COO and/or the price of in-patent product;(ii) the drug has been registered in a lower price in another GHC country;(iii) there is a change in the manufacturing site, and;(iv) the manufacturer requests this	✓
Egypt[2]	Lowest price	36	Algeria, Argentina, Austria, Bahrain, Belgium, Canada, Cyprus, Denmark, Finland, France, Germany, Greece, Hungary, India, Iran, Ireland, Italy, Japan, Jordan, Kuwait, Lebanon, Morocco, the Netherlands, Norway, Oman, Philippines, Poland, Portugal, Saudi Arabia, Spain, Sudan, Sweden, Switzerland, Turkey, UAE, UK	Public prices in basket countries	Manufacturers and public information sources (e.g. websites)	Every 5 years and when there are currency exchange fluctuations	✓
Jordan[2]	Median price	18[7,9]	Austria, Australia, Belgium, Croatia, Cyprus, Czech Republic, France, Greece, Hungary, Ireland, Italy, the Netherlands, New Zealand, Portugal, Spain, UK; plus COO as an	Public, ex-factory and CIF prices	Manufacturers, private sources and public information sources (e.g. websites)	Every 2 years, when there is currency exchange fluctuations or changes in currency exchange rates are taking place in the country of origin and in the reference basket	✓

	Price Calculation	Number of Basket countries	Countries in the Basket	Price source	Sources of information for pricing decisions	Price Revisions	Price adjustments
			option for the lowest price; plus Saudi Arabia as an option for the lowest price				
Kuwait	Lowest price[6]	5[6]	Bahrain, Oman, Qatar, Saudi Arabia, UAE	CIF price and retail price in basket countries	Manufacturer, public information, and private sources	When the price changes in key basket countries or in one of the GCC countries	-
Lebanon	Lowest price	15[7]	Bahrain, Belgium, UK, France, Italy, Jordan, Kuwait, Oman, Portugal, Qatar, Saudi Arabia, Spain, Switzerland, and the UAE; plus COO	CIF, wholesaler and public prices in basket countries	Manufacturers	Every 5 years and when the price changes in key basket countries	✓
Morocco[4,5]	Lowest price	7[7]	Belgium, France, Portugal, Saudi Arabia, Spain, Turkey; plus COO	Ex-factory price in basket countries	Manufacturers and public information sources (e.g. websites)	Every 5 years and when price changes in key basket countries	✓
Oman	Lowest price	>6[7,9]	GHC countries (Bahrain, Kuwait, Qatar, Saudi Arabia, the UAE); plus COO; plus countries where prices can be found in official references; prices of drugs in the same pharmacological group	Ex-factory, wholesale, export and retail prices	Manufacturers		-
Qatar	Lowest price	5[7]	COO, Bahrain, Kuwait, Oman, the UAE	CIF and public prices	Manufacturers; access to GCC CIF prices	When the price changes in key basket countries	-
Saudi Arabia	Lowest price	30	Algeria, Argentina, Australia, Bahrain, Belgium, Canada, Cyprus, Denmark, Egypt, France, Germany, Greece, Hungary, Ireland, Italy, Japan, Jordan, Kuwait, Lebanon, the Netherlands, New Zealand, Oman, Portugal,	Ex-factory and wholesale price in country of origin; public prices in country of origin and other countries where product is marketed; CIF price to Saudi in country of origin currency; CIF prices to	-	Every 5 years	-

	Price Calculation	Number of Basket countries	Countries in the Basket	Price source	Sources of information for pricing decisions	Price Revisions	Price adjustments
			South Korea, Spain, Sweden, Switzerland, Turkey, the UAE, UK;	countries in which product is marketed			
UAE	Median price	18	Austria, Bahrain, Belgium, Canada, Denmark, Finland, France, Germany, Ireland, Italy, Kuwait, the Netherlands, Norway, Saudi Arabia, Spain, Sweden, Switzerland, UK	Ex-factory, import price, CIF price in basket countries	Manufacturers and public information sources (e.g. websites)	Periodic reviews: all innovative and generic drug prices are revised every 5 years, along with the renewal of product registration; also when prices change in key basket countries Exceptional reviews: i) In case of expiry of an innovator's patent; ii) In case of any minor changes on the product; iii) Upon request of health authorities	×

Notes: [1] Price-cut is mandatory if France, UK, Belgium or Spain is the lowest price in the basket (primary evidence).

[2] If the drug is marketed in less than five countries, pricing should be done either following a comparative study between the product in question and its therapeutic alternatives, or as per the least of the prices in those five countries (Wanis, 2015).

[3] If it is not priced in all those countries, the median price where available in not less than four countries is used (Primary Evidence; El-Dahiyat and Curley, 2017).

[4] The country of origin is included in the basket when the price is different and when the price is equal to ex-factory price of country of origin if not launched in the basket countries (Primary Evidence).

[5] In Morocco the average price of the basket is considered for existing products contrary to the lowest price which is considered for new pharmaceuticals (Primary Evidence).

[6] According to primary evidence the Kuwaiti basket comprises a total of 30 countries of which the average is used to extract the reference price (Primary Evidence: Kuwait, 2018). The five countries included in the table (and the lowest price thereof) relate to the GHC basket.

[7] Figure includes country of origin (COO).

[8] In Bahrain, the figure does not include 'other countries' as specified in the latest version of the Pricing Guideline from the National Health Regulatory Authority (NHRA), of April 2017. Based on further primary data collection it appears that the basket of countries considered is the same as the one in Saudi Arabia.

[9] In Oman, the pricing criteria also include countries where prices can be found in official references (e.g. BNF), but these are not specified. An additional price-setting criterion includes prices of other drugs in the same pharmacological group.

[10] In Jordan, the ERP basket comprises 16 countries. The figure on this table includes (a) country of origin and (b) Saudi Arabia as potential pricing options, rather than as explicit basket countries: these two are presented within 4 pricing options for the lowest price (Price in COO, in KSA, across basket, or export price).

Key: '✓' = yes / used

'×' = no / not used

'-' = no evidence

Source: Adapted by the authors from the findings of both primary and secondary data collection.

5. Coverage and reimbursement policies and procurement

5.1. Reimbursement & Procurement

This section discusses the main mechanisms for procurement and reimbursement in each study country for in-patent, off-patent, and generic pharmaceuticals.

5.1.1. In-patent pharmaceuticals

The methods used for the procurement and reimbursement of in-patent drugs varies widely across the MENA region. Most countries employ a combination of mechanisms for reimbursement decisions. Two countries (Algeria, Morocco) depend primarily on negotiations for reimbursement decisions, which is accompanied by some kind of cost-benefit assessment or similar cost analysis, to inform reimbursement. The MENA region also relies on tendering or formulary management for procurement and reimbursement. The region is seeing an increasing move to the use of risk-sharing agreements, although this is a recent trend, which focuses exclusively on financial agreements. HTA, a systematic evaluation or assessment of the effect and/or impact of new health technologies, is not used widely in the MENA countries, but there are trends, such as the recently passed legislation on universal health insurance coverage in Egypt and Saudi Arabia's Vision 2030, where mention is made on HTA and efficiency either explicitly (Egypt) or implicitly (Saudi Arabia). Some countries, are using comparative clinical benefit assessment, occasionally combined with budget impact analysis or have a requirement for a 'token' cost-effectiveness study to be submitted for consideration by the competent authorities (Algeria, Morocco, Lebanon). The following paragraphs provide a short overview of the use of these methods in the study countries. **Table 8** provides an overview of the findings on mechanisms for procurement and reimbursement.

Table 8: Reimbursement and procurement mechanisms for in-patent medicines, 2018*

	IRP (molecular)	IRP (therapeutic)	IRP (managed competition)	ERP	HTA[1]	RSA[2]	Tendering	Formulary management	CCBA[3]	Negotia-tion	Budget Impact
Algeria	×	×	×	✓-	×	✓	✓[4]	✓[4]	✓	✓	✓
Bahrain	-	-	-	-	×	-	-	-	-	-	-
Egypt	×	×	×	×	×[5]	✓	✓	✓[4]	✓	✓	-
Jordan	-	-	-	-	✓-	×	✓	-	-	-	-
Kuwait	×	×	✓-	✓	×	×	✓	×	×	×	×
Lebanon	×	×	×	×	×	✓	✓	✓	×	✓	-
Morocco	×	×	×	✓-	×	×	✓	×	✓	✓	-
Oman	-	-	-	-	×	-	-	-	-	-	-
Qatar	×	×	×	✓-	✓[1]	×	✓	✓	×	×	×
Saudi Arabia	×	×	×	✓	×[5]	×	✓	✓	×	✓	-
UAE	×	×	×	×	×	×	×	✓	×	✓	-

Notes: * Applies to all medicines whether outpatient or in-patient; if relevant to out- or in-patient, a qualification is made where appropriate.
[1] The application of HTA is inconsistent and not systematic. It may be the case that national (pricing) guidelines specify that it may be necessary for countries to submit pharmacoeconomic evidence, but it is unclear whether this it taken into account or how.
[2] Primary data collection from a few settings suggested that RSA was being *considered* but this was likely to be relating to the future application of any RSA arrangements. Current legislative frameworks in the study countries do not allow RSA strategies to be implemented, particularly those of outcome-based RSAs.
[3] Comparative clinical benefit assessment. Although it has been mentioned that CCBA is applied as part of national legislation, it is unclear how robustly this is taking place and based on what methodology.
[4] Only used in hospitals, not at outpatient level.
[5] Not currently using but HTA planned to be implemented in due course based on passed legislation or current government initiative.

Key: '✓' = yes / used
'×' = no / not used
'-' = no evidence
'✓-' = Used as a reference price/guide and/or not necessarily in a systematic way.

Source: LSE based on primary and secondary data collection.

Negotiations based on ERP prices

In Algeria, Kuwait, Morocco, and Qatar, reimbursement prices are based on a form of negotiation between the manufacturer and the payer, but of course, the starting point for these negotiations is the ERP-derived price.

In ***Algeria***, reimbursement negotiations are based on prices fixed by the Pricing Committee through ERP assessments of in-patent molecules. The prices resulting from ERP are considered price caps for reimbursement price negotiations. Negotiations are conducted by the Reimbursement Committee, and can lead to three outcomes: (1) the aforementioned EPR price will be the reimbursement price with or without prescribing conditions; (2) a lower price for reimbursement is set (and endorsed by the Pricing Committee as the new list price) based on comparative clinical benefit assessment and/or on budget impact assessments; or (3) a reference tariff for reimbursement will be set on molecular or therapeutic basis with reference to cheapest alternative products already on the market. Primary data collection suggests that although the application of risk sharing remained aspirational until very recently, the Reimbursement Committee is allegedly committed to implementing a price-volume agreement programme by the end of 2018 and move to a type of performance agreements in 2019.[1]

In ***Kuwait, Morocco and Qatar***, ERP prices are often the starting point for negotiations or are used as a criterion to determine reimbursement of innovative drugs. Reimbursement negotiations look for a price decrease to negotiated/applied to the ERP price (Primary Evidence: Kuwait, Morocco, Qatar, 2018).

Cost-benefit analysis

Algerian reimbursement negotiations depend on comparative clinical benefit assessment as the main mechanism for assessing reimbursement coverage. In addition, budget impact is considered in reimbursement decisions as well, and the ERP-derived price may be retained as a reimbursement price where budget impact is considered to be limited (Primary Evidence: Algeria, 2018).

In ***Egypt***, the Egyptian Technical Committees (in place per therapeutic category) perform a comparative assessment between new, expensive products and the general standard of care guidelines. These assessments inform decisions for formulary listing. Cost-effectiveness analyses are used in reimbursement processes when requested by a

[1] The Reimbursement Committee is currently asked to consider cost-effectiveness of treatments in diabetes supported by local real-world data, and to consider more developed budget impact models for innovative therapies that include cost-savings related to complications and hypoglycaemia (for iSGLT2 and GLP-RA1).

manufacturer or deemed necessary by the Egyptian Reimbursement Committee. Clinical and economic value are also considered.

Reimbursement decisions are based on comparative clinical benefit assessments conducted by medical and/or scientific committees (Primary Evidence: Morocco, 2018). The reimbursement decision is also accompanied by a cost comparison with current practice or treatment: where innovative drugs have a higher price, the manufacturer is required to engage in one-to-one negotiations with the payer, possibly leading to a price review (Primary Evidence: Morocco, 2018).

Formulary management

Formulary management is a key tool aiding reimbursement in ***Lebanon, Qatar, Saudi Arabia, and the UAE***. In Algeria and Egypt formulary management is a method used by hospitals for drug procurement, but it is not used at a national level.

In Saudi Arabia, pharmaceuticals listed on the government formularies are reimbursed. Drug coverage decisions are largely made following the CCHI model, with other payers depending on medical committees, the health services provider, or a physician or pharmacist at the company. Private sector employees receive basic healthcare coverage from their employer, which covers some of the drugs on the Saudi National Formulary.

Tendering

Tendering is widely used across the region to procure pharmaceuticals paid for by the government sector. However, in certain cases (e.g. Algeria) tendering is solely used at hospital level, not at out-patient level.

In ***Egypt***, tendering remains the primary procurement mechanism through a Tender Drug List (TDL) system for products used within government facilities. The Ministry of Health procures around 70% of the total drug quantities through a central tender, 20% through local suppliers, and 10% is purchased from multinational manufacturers; notably, different institutions (e.g. hospitals have different tender mechanisms in Egypt (Primary Evidence: Egypt, 2018).

In ***Jordan***, tendering is also the primary system used: reimbursement in the Jordanian public sector is through an allocated budget of public sector institutions which is distributed to the unified purchasing department (JPD) to procure medicines for the public sector (Primary Evidence: Jordan, 2018).

In ***Morocco***, tendering is a secondary mechanism used for in-patent drugs based on therapeutic areas and where drugs with no off-patent/generic alternatives exist (Primary Evidence: Morocco, 2018).

Risk-sharing Agreements

There is increased interest in the use of RSAs in the MENA region for expensive, innovative products for rare diseases, but, to-date, the uptake is very limited, if at all. This is still an aspirational development for the entire region and it is doubtful that local legislative frameworks allow RSAs (particularly outcomes-based) to be implemented. In some settings, some developments around the introduction of RSA-like mechanisms has been reported; for example, in ***Algeria*** agreements between National Health Insurance bodies and pharmaceutical companies for expensive, innovative products were first introduced in 2017; the local Reimbursement Committee has ultimate decision-making power to implement RSAs in instances where the comparative clinical benefit is demonstrated for all indications, but the budget impact is considered high despite a lower negotiated reimbursement price. In ***Egypt***, agreements between industry and competent authorities generally result in discounts, but there currently are no outcomes-based agreements (Primary Evidence: Egypt, 2018). RSAs are also limited in ***Lebanon***: while currently used within the National Social Security Fund (NSSF), implementation of RSAs with other payers is still limited (Primary Evidence: Lebanon, 2018).

5.1.2. Off-patent pharmaceuticals

Table 9 provides an overview of main mechanisms for procurement and reimbursement for off-patent pharmaceuticals in the MENA region. Tendering is the most prevalent mechanism for the procurement of off-patent pharmaceuticals, used in six countries (Egypt, Kuwait, Lebanon, Morocco, Qatar, Saudi Arabia, and the UAE). The table also shows tendering is generally used in combination with internal reference pricing (Morocco, Qatar), CBA (UAE, Qatar), and formulary management (Algeria, Lebanon, Qatar, Saudi Arabia). The exception is Egypt, which relies solely on tendering through its public procurement system.

Outliers are Algeria and Qatar. Algeria, relies on a variety of methods. In ***Algeria***, IRP at both molecular and therapeutic level, and formulary management are used, though the main mechanism for assessing reimbursement coverage is comparative clinical benefit assessment, and tendering and formulary management are used chiefly or solely within hospitals. Molecular or Therapeutic Reference Pricing are used to set reference tariffs for reimbursement. ERP prices provide the basis and ceiling for price setting in

reimbursement. In ***Qatar*** a combination of IRP at molecular level, ERP, formulary management, and bio-equivalence are used (Primary Evidence: Qatar, 2018).

Tendering & formulary management

In ***Saudi Arabia***, both a centralized and decentralized procurement system exists. The centralized procedure is conducted through the National Unified Procurement Company (NUPCO). The decentralized mechanism allows specific institutions such as the MoH and National Guard (one of the three main branches of the Saudi Army) to procure for their needs, though often tense only allows manufacturers to bid if their brand is included in their formulary (Primary Evidence: Saudi Arabia, 2018).

Table 9: Reimbursement and procurement mechanisms for off-patent medicines, 2018*

	IRP (molecular)	IRP (therapeutic)	IRP (managed competition)	ERP	HTA[1]	RSA	CCBA	Tendering	Formulary management
Algeria	✓	✓	×	✓-	×	×	×	✓[2]	✓[2]
Bahrain	-	-	-	-	-	-	-	-	-
Egypt	×	×	×	×	×	×	×	✓	×
Jordan	-	-	-	-	-	-	-	-	-
Kuwait	×	×	×	×	×	×	×	✓	×
Lebanon	×	×	×	×	×	×	×	✓	✓
Morocco	✓	×	×	×	×	×	×	✓	×
Oman	-	-	-	-	-	-	-	-	-
Qatar	✓	×	×	✓-	×[1]	×	×[3]	✓	✓
Saudi Arabia	×	×	×	×	×	×	×	✓	×
UAE	×	×	×	×	×	×	×	✓	×

Notes: * Applies to all medicines whether outpatient or in-patient; if relevant to out- or in-patient, a qualification is made where appropriate.
[1] Currently there is no HTA is inconsistent and not systematic.
[2] Only used in hospitals, not at out-patient level.
[3] In general, the application of CCBA is inconsistent and not systematic; it is not relevant for off-patent medicines.

Key: '✓' = yes / used.
'✓-' = used as a reference price for guidance.
'×' = no / not used.
'-' = no evidence.

Source: LSE based on primary and secondary data collection.

5.1.3. Generic pharmaceuticals and biosimilars

Generic pharmaceuticals and biosimilars are making an increasing component of the market in the study countries. Generics have been on the market much longer than biosimilars, but the latter are making inroads into several of the study countries.

Table 10 provides an overview of main mechanisms for procurement and reimbursement for generic pharmaceuticals in the MENA region. As with the procurement and reimbursement of off-patent pharmaceuticals, tendering is the most prevalent mechanism for the procurement of generic pharmaceuticals, used in seven countries (***Algeria, Egypt, Kuwait, Lebanon, Morocco, Qatar, Saudi Arabia, and the UAE***). The findings show a number of countries use this in combination with other mechanisms: IRP (Algeria, Lebanon, Morocco, Qatar) and formulary management (Algeria, Lebanon, Qatar, Saudi Arabia). Egypt and the UAE rely solely on tendering.

In ***Algeria***, internal reference pricing (molecular and therapeutic) is used to set the reference tariff for reimbursement. Generics and biosimilars are automatically reimbursed according to their fixed price where the originator with the same active substance received a prior positive decision and is already reimbursed. Where the generic or biosimilar is the first to come on the market, budget impact criteria and ERP is used for reimbursement (Primary Evidence: Algeria, 2018). Tendering and formulary management is only used within hospitals.

Reimbursed prices for generics in the ***UAE*** vary according to the country of manufacture: generics manufactured in the UAE or other GCC members are reimbursed at 20% below the originator price, while imported generics are priced at 30% below the originator price (Abuelkhair et al., 2012). In ***Qatar*** the prices of generic medicines are set based on some notion of molecular reference pricing (Primary Evidence: Qatar, 2018).

Biosimilars have already started making inroads to most MENA countries. For instance, biosimilars contribute to more than 40% of the total biologics market in Lebanon, while in Egypt and the UAE, biosimilars have already penetrated into key biologics space and currently contribute to approximately 14% and 5% respectively of the biologics market (QuintilesIMS, 2017). Pricing and market access levers are key to ***Saudi Arabia*** being the biggest market for biologics in the MENA region and was the first to implement a distinct regulatory route for biosimilars in 2010 following the guidelines issued by the EMA, which led to the registration in Saudi Arabia of the biosimilars filgrastim (Hospira), epoetin alfa (Sandoz) in 2015 and Remsima (Celltrion) in 2016; these are expected to open the door for the entry of other biosimilars (QuintilesIMS, 2017). Other countries in the region are

also preparing themselves commercially and technically to create space for biosimilar adoption. ***Jordan's*** first biosimilar was approved in 2009 following the EU guidelines and now has its own regulatory guidelines approved. ***Algeria***, despite nascent regulatory framework, is seeing more and more biosimilar reaching the market (i.e., Hikma is in the final phases of registration of trastuzumab). Depending on the channel of negotiation, biosimilars can cost 30-50% less compared to the originator biologic; in fact, in some markets such as Lebanon and Egypt, the difference may go up to 70-80% especially for erythropoetin and filgrastim biosimilars.

Algeria, Egypt, Morocco, Saudi Arabia, and the UAE are countries with significant biosimilar potential as they have developed their own regulatory guidelines and are approving biosimilars. The challenges facing suppliers are not dissimilar to the challenges posed by the regulatory environments in these countries and relate – mainly – to the conduct of clinical trials and the timeliness of regulatory approvals.

Table 11 summarises the available evidence on the existence or not of regulatory guidance and the time to market.

Table 10: Reimbursement and procurement mechanisms for generic medicines*

	IRP (molecular)	IRP (therapeutic)	IRP (managed competition)	ERP	HTA	RSA	CCBA	Tendering	Formulary management	Bio-equivalence
Algeria	✓	✓	×	×	×	×	×	✓[1]	✓[1]	×
Bahrain	-	-	-	-	-	-	-	-	-	-
Egypt	×	×	×	×	×	×	×	✓	×	×
Jordan	-	-	-	-	-	-	-	-	-	-
Kuwait	×	×	×	×	×	×	×	✓	×	×
Lebanon	✓	✓	✓	×	×	×	×	✓	✓	✓
Morocco	✓	×	×	×	×	×	×	✓	×	×
Oman	-	-	-	-	-	-	-	-	-	-
Qatar	✓	×	×	×	×	×	×	✓	✓	✓
Saudi Arabia	×	×	×	×	×	×	×	✓	×	×
UAE	×	×	×	×	×	×	×	✓	×	×

Notes: * Applies to all medicines whether outpatient or in-patient; if relevant to out- or in-patient, a qualification is made where appropriate.
[1] Only used in hospitals, not at out-patient level.

Key: '✓' = yes / used
'✓*' = only used in hospitals, not at national level
'×' = no / not used
'-' = no evidence

Source: LSE based on primary and secondary data collection.

Table 11: The extent of biosimilar readiness in MENA countries

	Available regulatory guidance	Time to market (in months)
Algeria	✗[1]	24
Bahrain	n/a	n/a
Egypt	✓	8 - 10
Jordan	✓	6 - 12
Kuwait	✗	6 - 24
Lebanon	✗[1]	6 - 12
Morocco	✓	24
Oman	n/a	n/a
Qatar	n/a	n/a
Saudi Arabia	✓	18
UAE	✓[2]	12 - 18

Note: [1] Exist in draft.

[2] Not published as of 2017.

Key: '✓' = yes
'✗' = no

Source: Adapted from QuintilesIMS, 2017.

5.2. Generic prescribing and substitution

Table 12 presents findings on generic prescribing and substitution across the study countries. Generic prescribing policies seek to contain costs where physicians are encouraged or required to prescribe by international non-proprietary name (INN), rather than a brand-name drug. Policies formalizing this practice as mandatory exist only in four of the study countries: ***Jordan, Oman, Qatar, and the UAE. Algeria*** and ***Lebanon*** have policies encouraging generic prescribing. Out of all the countries with any kind of policy on generic prescribing, none has implemented an electronic system to manage the practice.

Generic substitution policies are a form of cost-containment, allowing pharmacists to dispense a different brand or an unbranded drug product instead of a branded drug prescribed by a physician. Most countries in the MENA region have a generic substitution policy in place, with the exception of Bahrain, Morocco, and Qatar. However, only in Jordan is generic substitution mandatory, while the remainder of the countries (Algeria, Egypt, Kuwait, Lebanon, Oman, Saudi Arabia, and the UAE) only have policies or legislation which encourages or strongly encourages the practice.

Other practices observed include efforts to encouraged insurers to pay for the cheapest generic drug(s), requiring the patient to pay the difference if they choose to use a branded product (seen in Morocco; BMI, 2017d, 2016d).

The results on **Table 12** should be interpreted with caution. While the table depicts policies and practices in the region that may be included in national legislation, it is unknown how widely they are implemented. Indeed, the fact that consumption of pharmaceuticals in the region is predominantly centered around branded products, highlights two key concerns with generics, particularly certain imported products: first, there is often an issue of trust amongst prescribers as well as consumers/patients on generics, due to the possibility of substandard and/or counterfeit products entering the supply chain; and, second, partly as a result of the deficit in trust, prescribers are in a position to make suggestions to consumers on brands which, in their view meet those quality standards. Overall, it appears that significant effort needs to be made for generics to be accepted by several of the countries in the region, particularly in terms of improving quality standards.

Table 12: Generic Prescribing and Substitution*

	Generic prescribing			Generic dispensing/substitution	
	Is there a generic prescribing policy in place?	Is generic prescribing mandatory or encouraged within existing policy? [2] (*n/a for countries with no relevant policies*)	For mandatory generic prescribing policies, is there an IT system? ('-' *for non-mandatory systems*)	Is there a generic substitution policy in place?[2]	Is generic substitution mandatory or encouraged?[2] (*n/a for countries with no relevant policies*)
Algeria	✓	Encouraged	-	✓	Encouraged/mandatory
Bahrain	NA	Not mandatory	-	NA	NA
Egypt	×[1]	NA	-	✓	Encouraged
Jordan	✓	Mandatory[3]	No	✓	Mandatory (public sector) [3]
Kuwait	NA	Encouraged/Not mandatory	-	✓	Encouraged (public sector) [3]
Lebanon	✓	Encouraged	-	✓	Encouraged
Morocco	✓	NA	NA	NA	NA
Oman	✓	Mandatory (public sector)[3]	NA	✓	Encouraged (public sector) [3]
Qatar	✓	Mandatory[3]	NA	×	n/a
Saudi Arabia	NA	Not mandatory	-	✓	Encouraged
UAE	✓	Mandatory (public sector) [3]	NA	✓	Encouraged

Note: * The results capture what official policies may suggest; in practice, generic prescribing may be overridden by prescribers suggesting a brand and, more importantly, both generic prescribing and substitution policies are poorly implemented as trust on generics is often problematic due to likely substandard or counterfeit generics.

NA: not available.

[1] There may not be an explicit generic prescribing policy in place, nevertheless, there is a generics policy in place with the wider name of 'generics box'.

[2] Both columns reflect current policies as stated in legislation. However, due to the likelihood of poor quality products entering the market in many cases, it is not known how widely these policies are implemented in practice.

[3] Not known how widely implemented this is.

Source: LSE based on primary data collection.

6. Industrial policies – Support of local and international industry

6.1. Manufacturing activities

Local manufacturing includes local manufacturers, and contract manufacturing of licensed pharmaceuticals by multinational manufacturers. Multinational manufacturing includes imports of final products, and local subsidiaries of foreign/international companies engaged in manufacturing and sales activities. **Table 13** provides a summary of the available evidence on manufacturing activities in the study countries by local companies, and activity by non-domestic entities.

Table 13: Summary of evidence on the state of the art in local manufacturing activities

	Evidence on manufacturing by local companies	Evidence on activity by non-domestic entities
Algeria	▪ Domestic pharmaceutical production is experiencing robust growth (BMI, 2017a).	▪ Multinational manufacturers have the largest market share in value terms (BMI, 2017a, 2016a). They mainly engage through imports (BMI, 2017a). ▪ The majority of Algeria's pharmaceutical consumption originates from imports (Zerhouni and El Alami El Fellousse, 2013).
Bahrain	▪ Generic pharmaceutical sector development is limited by narrow local production (BMI, 2017j). ▪ The small manufacturing industry is unlikely to be manufacturing a diverse patented selection of pharmaceuticals (Anonymous, 2010). Therefore, without private or government investment, expansion potential is limited (Anonymous, 2010).	▪ Mainly relies on imports in the generic pharmaceutical sector (BMI, 2017j). ▪ Imports most of its medicines from France, Germany, UK, Switzerland and US (Anonymous, 2010)
Egypt	▪ Domestic manufacturing is not so limited: - There are 119 pharmaceutical manufacturers (WHO, 2011, 2011a). - Egypt does not have R&D to discover new active substances, but it does produce APIs (WHO, 2011, 2011a). - National pharmaceutical industry covers 92-94% of market needs by volume, and 82% by value (Mohamed, 2014)[2].	▪ 18 multinational companies manufacture pharmaceuticals locally (WHO, 2011, 2011a). ▪ Importing companies address 6-8% of needs, so c.7% volume and they comprise 18% of market value (Mohamed, 2014). ▪ Imports many raw materials and highly specialised pharmaceuticals. Imports c.85% of chemical compounds, raw materials & active ingredients (Mohamed, 2014).
Jordan	▪ Domestic manufacturing is not so limited: - Contributes 25% by value to the total pharmaceutical market (WHO, 2007). - Has R&D to discover new active substances, and produces APIs (WHO, 2011b) - Only country in the region which has a positive pharmaceutical trade balance (BMI, 2017). - C.5% of local production is produced under license agreement with brand manufacturers (Al-Abbadi, 2009).	▪ Imported medicines dominate consumption, given preference for branded medicines (BMI, 2017; WHO, 2007). ▪ C.74% of pharmaceuticals are imported (Al-Abbadi, 2009).

[2] According to another source, national pharmaceutical industry covers 93% of market (64).

	- Expanding local industry with capacity to export (WHO, 2007).	
Kuwait	▪ Less than 25% of pharmaceuticals in volume terms are locally produced (BMI, 2017g). ▪ 1 pharmaceutical company which produces generics, some under licensing agreements with multinational companies (Ball et al., 2005).	▪ Imports comprise most of the volume and value demand (BMI, 2017g, 2016f).
Lebanon	▪ Domestic manufacturers produce 5% of market share by volume (WHO, 2012a). ▪ The 7 local manufacturers operate only to 25% of their capacity (WHO, 2009a). ▪ Does not have R&D to discover new active substances and does not produce APIs (WHO, 2012a).	▪ 25 multinational pharmaceutical companies manufacture medicines locally (WHO, 2012a). ▪ Most registered medicines (including high-priced pharmaceutical specialties) are imported, mainly from USA and Europe (WHO, 2006b, 2009a).
Morocco	▪ Comprises 40 production units (Zerhouni and El Alami El Fellousse, 2013). ▪ Local production caters for 80% of needs (WHO, 2006c). ▪ Modest exports to some Arabian, African, and European countries (WHO, 2006c).	▪ C.100% of active materials and c.50% of conditioning articles are imported (WHO, 2006c).
Oman	▪ Does not have R&D to discover new active substances but does produce APIs (WHO, 2011c). ▪ There are three local manufacturers[3], only one of which manufactures raw materials (WHO, 2015).	▪ Most registered pharmaceuticals are imported, mainly from Europe, India, USA, and other Arab countries (WHO, 2015).
Qatar	▪ 1 licensed pharmaceutical manufacturer (Awaisu et al., 2014; WHO, 2011e). ▪ Does not have R&D to discover new active substances and does not produce APIs (WHO, 2011e).	▪ Imports comprise 97% of pharmaceutical market (BMI, 2017i). ▪ Highly import-dependent, due to small market size which means there is limited interest in developing manufacturing plants in Qatar (Awaisu et al., 2014; Ibrahim, 2015). Preference for imports from western countries, and a small fraction from MENA and Asian countries (Ibrahim, 2015). ▪ No foreign manufacturers directly manufacture in the country, even though some e.g. Novartis have local offices (BMI, 2017i).
Saudi Arabia	▪ Domestic manufacturers had 18% of market share by value produced in 2012 (Alkhuzaee et al., 2016)[4]. ▪ Local companies produce c. 20% of domestic pharmaceuticals. A significant proportion of these are	▪ KSA depends on imported pharmaceuticals (Alkhuzaee et al., 2016; BMI, 2017f; Khan et al., 2016; PR Newswire, 2013) from developed countries (BMI, 2017f). ▪ 4 multinational companies manufacture pharmaceuticals locally (Alkhuzaee et al., 2016; WHO, 2011f, 2012b)

[3] According to an earlier source, there are 4 pharmaceutical manufacturers in Oman (75).
[4] Domestic manufacturers had 20% of the market share by value produced in 2011 (80, 81).

	patented pharmaceuticals licensed from multinational manufacturers, not generics (BMI, 2016e). ▪ Domestic manufacturing industry comprises 15% of market expenditure (BMI, 2016e) ▪ Does not have R&D to discover new active substances and does not produce APIs (WHO, 2011f).	▪ Multinationals are indirectly involved even if they are not present in KSA's market, as shown by the contract manufacturing (BMI, 2017f) of patented pharmaceuticals by local companies under license agreements (BMI, 2016e, 2017f). Significant amount of local activity will continue as manufacturing under license (BMI, 2016e, 2017f). ▪
UAE	▪ Domestic pharmaceutical industry is small (BMI, 2017h). ▪ There are 10 licensed pharmaceutical manufacturers (WHO, 2012c). ▪ Does not have R&D to discover new active substances, and does not produce APIs (WHO, 2012c)	▪

Source: LSE from primary and secondary data sources.

As Table 13 shows, there is generally limited domestic manufacturing, and significant multinational activity across the study countries. In the region, international companies are setting up local manufacturing facilities, and are more likely to have a direct presence within the Gulf States because of infrastructural advantages (BMI, 2017k). Across the region, there is dependence on branded (both off- and in-patent) pharmaceutical imports, especially in the GCC states (Ibrahim, 2015). In the latter, 75% of all pharmaceuticals are imported from other countries (Tribune Business News, 2013).

Another trend across the region (with few exceptions), most governments are focused on decreasing their import dependence, and are promoting local pharmaceutical production and import substitution (BMI, 2017k). Many countries are increasing local production through engaging in contract manufacturing agreements between multinational and local companies to produce treatments, for example in chronic disease (BMI, 2017k). In GCC states, attempts have been made to develop pharmaceutical facilities together with multinational manufacturers (Tribune Business News, 2013). In Kuwait, Japanese companies have entered the market through joint ventures (BMI, 2017g). In Algeria, the government is attempting to enhance local production through joint ventures (BMI, 2017a, 2016a).

6.2. Supporting local and foreign manufacturers

Tables 14 and 15 analyse the key trends in the support provided to local and multinational manufacturers respectively. Support provided to local manufacturers includes direct support, and discriminatory practices towards multinational manufacturers, such as procurement and pricing policies favouring local manufacturers. Support is categorised as: tax breaks/exemptions and subsidies, registration, reimbursement, pricing incentives, and importation.

6.2.1. Support of local manufacturing activities

Table 14: Support for local manufacturers

	Taxation/ subsidies	Registration	Reimbursement	Pricing	Importation
Algeria	✓	-	✓[1]	-	-
Bahrain	✓	-	✓	-	-
Egypt	-	-	✓	✓	-
Jordan	-	✓	✓	✓	-
Kuwait	✓	-	✓	-	-

Lebanon	-	-	✓	-	-
Morocco	-	-	✓	-	✓
Oman	-	-	-	✓	-
Qatar	-	-	✓	-	-
Saudi Arabia	✓	-	✓	✓	✓
UAE	-	-	-	✓	-

Note: [1] Local manufacturing is a necessary activity if reimbursement is to be granted.

Key: '✓' = yes/ used
'–' = no evidence

Source: LSE from primary and secondary data sources.

Taxation/subsidies

Saudi Arabia, Algeria, Bahrain, and Kuwait employ taxation/subsidy policies to maximise local production. In Saudi Arabia, support is provided to domestic manufacturers through free property leases, and interest-free loans (BMI, 2016e). In Algeria and Saudi Arabia, the government provides subsidies (BMI, 2017a, 2016a, 2016e). In Bahrain, there is a regime of tax exemption for ten years (BMI, 2017j). In Kuwait, tax exemptions are provided to local manufacturers (Primary Evidence: Kuwait, 2018).

Registration

In Jordan, registration is biased in favour of locally procured pharmaceuticals, given they face lower registration fees than imported pharmaceuticals (Bader et al, 2007).

Pricing

To encourage their production, local generics achieve more beneficial pricing arrangements than foreign generics (Saudi Arabia, UAE, and Egypt). In Saudi Arabia and UAE, local generics achieve a lower percentage markdown off originator prices, than foreign generics (Qarain et al, 2009). In Egypt, imported generics' prices are based on the availability of similar generics in Egypt and local generics' date of pricing (Egypt) (Qarain et al, 2009).

In Jordan, Morocco, Oman, and Saudi Arabia, there are other forms of pricing discrimination against imported pharmaceuticals to maximise local production. There is discrimination against some imported pharmaceuticals in the form of their delayed market entry owing to lengthy price negotiations (Jordan) (BMI, 2017), high levels of government control (Morocco, Oman, Saudi Arabia) (BMI, 2017e; PR Newswire, 2013) whereby new products are being given some of the lowest prices in the region (Oman) (BMI, 2017e).

In Saudi Arabia, there may be elements of preferential price treatment received by foreign companies. Pharmaceuticals manufactured under license, under patent and priced for the licensor company are given the same price awarded to the licensor; pharmaceuticals manufactured under license, under patent and introduced through a domestic manufacturer are priced in line with the 'common pricing criteria'; pharmaceuticals manufactured under license, under patent and manufactured locally under the name assigned by the domestic manufacturer (second brand), achieve a price 10% below the awarded price for the licensor company (Qarain et al., 2009).

Reimbursement

Bahrain, Egypt, Jordan, Kuwait, Lebanon, Morocco, Qatar, and Saudi Arabia, use favourable procurement policies for local manufacturers. In public procurement, there are provisions which give priority to local manufacturers' products (Saudi Arabia, Egypt, Jordan, Bahrain, Kuwait, Morocco, Lebanon, Qatar) (BMI, 2017c, 2016c, 2017i; WHO 2008, 2011, 2011a, 2011b, 2011f, 2012, 2017). This may also include favoritist practices in procurement and tenders, whereby locally manufactured products can win a tender even if the price submitted is up to 10% higher than the lowest submitted price (Egypt, Saudi Arabia) (Primary Evidence: Egypt and Saudi Arabia, 2018). In Algeria, local manufacturing is mandatory if reimbursement is to be granted.

Importation

Saudi Arabia, Morocco and Algeria use importation policies which discriminate against foreign manufacturers, to maximise the impact of local production. For example, a 5% import tariff is imposed on imports to the GCC (BMI, 2016e). Morocco has had an industrial policy built on the import substitution model since 1960 (Zerhouni and El Alami El Fellousse, 2013). In Algeria, there is an importation ban on foreign company imports into the country when 3 or more generics are available.

6.2.2. Support of multinational manufacturing activities

Table 15: Support for multinational manufacturers

	Taxation /subsidies	Registration	Reimbursement	Pricing	Importation
Algeria	-	-	✓	-	-
Bahrain	✓	-	-	-	-
Egypt	-	-	-	-	-

Jordan	-	-	-	-	-
Kuwait	✓	-	-	-	-
Lebanon	-	-	-	-	-
Morocco	✓	-	-	-	-
Oman	-	-	-	-	-
Qatar	✓	-	-	✓	-
Saudi Arabia	✓	-	-	✓	-
UAE	-	-	-	-	-

key: '✓' = yes/ used
'–' = no evidence

Taxation/subsidies

In Saudi Arabia, Bahrain and Morocco, foreign investment is encouraged through a variety of trade agreements (BMI, 2017d, 2016d, 2017j). In Kuwait, Saudi Arabia, and Qatar, foreign companies are supported through favourable tax regimes and subsidies. Multinational investment is supported by tax exemptions (Kuwait) (BMI, 2017g); free property leases, government subsidies and interest-free loans for multinational subsidiaries (Saudi Arabia) (BMI, 2016e); and parks which operate as free trade zones, providing tax-free operations, unrestricted profits, capital repatriation, and 100% foreign company ownership (Qatar) (BMI, 2017i).

Reimbursement

In Algeria, reimbursement policies encourage (indeed, they may necessitate) foreign investment in pharmaceuticals. Foreign firms must invest in Algeria if they are to be granted reimbursement. A total ban on foreign (imported) medicines is imposed if three or more generic options are available in the country. Foreign companies may be exempted from this rule if they have committed to investing or have already invested in the country (BMI, 2016a).

Pricing

In Qatar, pharmaceutical retail price control by the government enables importers to determine their own prices, following the dissolution of Law No.7 in 1990 (Awaisu et al., 2014).

7. Pricing and reimbursement in MENA countries: A synthesis

7.1. Issues relating to pharmaceutical pricing policies in the MENA region

7.1.1. Pricing policies and ERP

The dominance of ERP: Across the MENA region prices of in-patent pharmaceuticals are set based on various criteria, including the price in the country of origin of the pharmaceutical, the prices in the GCC region (where applicable), the therapeutic significance of the drug, the prices in official references such as the British National Formulary, if available, and the prices of pharmaceuticals under the same therapeutic category; however, the dominant criterion to inform pharmaceutical prices particularly for new products is ERP.

Formal value assessment: There is no formal value assessment system in operation explicitly in any of the MENA countries along the lines of an HTA system based on clinical and cost-effectiveness analysis or comparative clinical benefit assessment. These systems are still in an aspirational sphere for all the countries in the region, although Egypt and Saudi Arabia have moved closer to their implementation through recently passed legislative pieces (Egypt), or demonstrating their intent to move into that direction (Saudi Arabia). Of all the countries in the region some (selective) use of economic analysis was mentioned in Lebanon, Morocco and Egypt, but the instances in which this is used remains limited. Whatever value-based pricing system these countries will adopt in the future, special focus should be given to a) transparent criteria; and b) clear implementation mechanisms.

Price formation through ERP: Across the study countries the reference price for newly launched pharmaceutical products is calculated based on the lowest price in the basket. The consequence of this practice is that, in combination with exchange rate policy and frequent re-pricing (where it exists), pharmaceutical prices converge downwards over time, rather than remaining constant in real terms.

Reference baskets: Reference baskets tend to vary in the MENA region from small baskets such as in Qatar, Kuwait and Oman, which reference the GCC region, to very large baskets such as those in Egypt and Saudi Arabia. The larger the basket of reference countries, the more complex it becomes to administer an ERP system and the longer the delays in launching new products this practice may be associated with. As the majority of country baskets rely on low-price countries and/or setting prices based on the lowest in the basket, there is no meaningful notion of value assessment (e.g. based on additional

therapeutic impact or other criteria) of new products and their implications or importance in the countries in which they are introduced. Also, the current fast track/abridged licensing regulatory approval in the four key markets (UAE, Saudi Arabia, Jordan and Egypt) constitute an important factor to consider in relation to the reference basket, as repetitive referencing adds to administrative complexity and impacts price stability.

Availability issues: The way in which ERP is implemented in a country might have an additional impact on the availability of pharmaceuticals in that country. This is due to ERP policies, which are most likely to take place in highly regulated and/or small markets. Countries with flexibility on pricing, or markets that are large in size, with higher GDP per capita, and/or with increased public healthcare spending, a higher percentage of GDP on health expenditure and a higher price level of pharmaceuticals are less likely to suffer from reduced availability.

Spillover effects: During the design phase of ERP governments are likely to focus on the short-term financial gains that could be the result of a newly implemented ERP system that uses a "lowest price in the basket" style calculation. However, such decisions could negatively impact healthcare systems in the long term. From a policy perspective, EPR in itself does not restrict access once agreement has been reached but can lead to delays in launch, which, in itself can cause access problems. It can also be the case that manufacturers will not launch in a particular ERP market if they feel that the price they receive from that market is prohibitively low and can threaten their global pricing strategy.

Path dependency: There is an element of "path dependency" characterizing ERP systems in the sense that the information used in decision-making processes and the way it is arrived at, influences the final outcome to a certain degree. For instance, the type of data required from a particular scheme influences price levels, e.g. country selection, available prices from across the country basket, revision dates. To that end, ERP seems to be relying a lot on external factors influencing pricing (and reimbursement) decisions, without necessarily paying due attention to factors intrinsic to the health care system in which it operates.

Administrative complexity: In its simplest form, ERP is not an administrative complex system and, in the majority of cases, it relies on available information that can be obtained at arms' length. Nevertheless, the view that seems to emerge from meetings and interviews with stakeholders that the administrative process is quite complicated and resource intensive, not least because "there is a requirement to produce evidence on and validate every claim made along the way". Complexity is also directly related to the size of baskets and the frequency of re-pricing. Therefore, it is the intensity of information required often makes ERP schemes administratively complex.

Transparency: From a country's perspective it is important to ensure that ERP systems are transparent; this is important in order to ensure its perceived credibility among the stakeholder community. In this spirit, systems of ERP should not take into consideration rebated or discounted prices, even if there is an opportunity for these to be identified. These prices are not always fully transparent and, therefore, not defensible before the stakeholder community.

Value of innovation: In the majority of cases, the operation of an EPR scheme does not take into account the value of innovation. For instance, an issue arises when ERP is combined with molecular or therapeutic price referencing, the latter being a frequently-used option setting a reference price across a range of molecules, of which at least one is patent-expired. It is likely that these two effects can be combined and can spill-over across borders. The propagation mechanism for this to take place is differences in patent term dates across countries. Under these circumstances, it is probable that the patent for a product in one country may expire earlier than in others. This would, of course, allow generics to enter in the country where the patent expires and could force the originator price to decline particularly if an internal price reference system is in place. This decline may trigger price adjustments in other countries if the product in question is subject to ERP provisions elsewhere. To that end, such patent term differences across countries can have unintended consequences and lead to cross border price reductions if combined with internal price referencing elsewhere. Additionally, it is important to have in mind that the value of innovation could not be taken into account without proper generation of local data, such as burden of disease, incidence and prevalence. In that context, capability and capacity building is also an important component.

Stability: The timing of revisions should be selected carefully to create a stable price environment that stimulates manufacturers to invest in the launch of their products. If ERP takes place biennially and the lowest in the basket is selected, this almost certainly leads to a race towards the bottom. The study countries fare well on this front as, in most cases, re-pricing occurs every 3-5 years, leading to the least possible disruption or instability.

Exchange rate adjustments: Countries tend not to account for dynamic changes in exchange rates or reference country wealth differences, based on GDP or PPP, especially, if countries with stronger currencies or higher incomes per capita are used as reference. Often, the exchange rates used are unrealistic (e.g. a historically fixed exchange rate, which is no longer valid) and can offer a significant discount to newly launched products; the effect could be that products might not be launched anticipating a weak exchange rate and, therefore, a lower than expected reference price.

Addressing exchange rate volatility: Appropriate exchange rates are essential in ensuring realistic prices rather than prices arising from (excessive) exchange rate volatility. Arguably, both manufacturers and insurers wish to operate in a predictable environment that also provides stability. Exchange rate volatility (particularly depreciation) can also lead to product shortages on the market (Egypt has suffered on this front fairly intensely over the past year due to the depreciation of the Egyptian pound). In order to limit the effect of exchange rate volatility, either a fixed exchange rate could be negotiated at the point of pricing decisions based on historical trends, or some kind of moving average over an adequate period of time could be set.

Patent status issues: The use of therapeutic referencing to inform pricing decisions that are also informed by EPR may lead to distortions due to differences in intellectual property rights among countries. Finally, caution should be exercised when referencing in-patent products with generic medicines, in the context of combining ERP with internal price referencing at therapeutic class level.

In-patent product registration and pricing renewal process: In-patent product registration is often lengthy and time consuming and so is the pricing or price renewal process. Because the two processes (registration and pricing) are in many cases inter-connected and the achievement of the latter leads to the completion of the former, the delays are often significant, impacting access. While a separation of pure regulatory processes from pricing and/or reimbursement seems desirable, it is unlikely to lead to a long-term solution where the problem persists, unless a more streamlined pricing process is in place.

7.1.2. MENA ERP systems vs. ERP best practice

Based on our findings from the systematic literature review and primary evidence, we endeavoured to showcase whether the study countries follow the 14 best practice principles. **Table 16** below presents the extent to which countries comply with the principles and comes as a result of extensive consultation with local stakeholders and decision-makers as well as field visits that enabled to obtain a view of the operating environment as distinct from the prevailing regulatory framework in different study countries. This consultation has showcased in a number of good practice cases in the region, specifically, the UAE, Saudi Arabia, and Jordan (the latter to a lesser extent), although differences exist between the three of them and the extent to which they subscribe to individual principles (Table 16).

Overall, none of the countries in question seemed to follow all 14 of the ERP best practice principles with most failing to use the mean price of the basket and an administratively

simple and transparent system which involved stakeholder participation. Most countries use the lowest price in the basket, have large baskets, reducing administrative simplicity. Similarly, whilst external stakeholders may be consulted, their contribution to the actual decision-making related to ERP seems to be very restricted, as it is an administratively driven process that excludes stakeholder active participation. Further, despite stipulations about avoiding the impact of exchange rate volatility and keeping price revisions to a minimum, many of the countries in the region revise prices if there exchange rate fluctuations or if prices change in basket countries. The patterns shown on Table 16 seem to have some broad positive association with income per capita, in that the higher income per capita is, the greater the adherence to the 14 best practice principles. This is not surprising as high income is a predictor of less reliance on cost minimisation practices.

As highlighted earlier, the UAE and Saudi Arabia seem to have put in place provisions enabling them to adhere to several of the best practice principles, such as respecting patent status, focusing on in-patent drugs, avoiding impact of exchange rates, minimising price revisions, enable appeals, using ex-factory prices; in addition to the above, the UAE satisfies the principles of administrative simplicity, appropriate country selection and the use of mean prices. At the other end of the spectrum, Egypt and Algeria have systems in place that require significant interventions to be perceived as satisfying some of the key principles of ERP best practice.

Table 16: External Price Referencing in MENA Countries: Adherence to the 14 Best Practice Principles

	GDP per capita, 2017 adjusted for PPP$	Clear objectives aligning with policy goals	Focus on in-patent drugs only	ERP prices do not override HTA decisions	Administratively simple and transparent	Stakeholder participation	Possibility to appeal	Appropriate country selection	Consideration of international implications	Use of ex-factory prices	Use of mean prices	Respect of patent status	Avoid impact of exchange rate	Price revisions to a minimum	Alignment with negotiation tools
Algeria	15,050	✓	×	N/A	×	×	×[1]	×[1]	×[1,2]	✓	×	×[1]	×	×	×
Bahrain	42,930	×	✓	N/A	✓	×	✓	✓	×	✓	×	✓	×[1]	×	×
Egypt	11,360	×	×	N/A	×	×[1]	×[1]	×	×	×	×	×[1]	×[1]	×	✓
Jordan	9,110	✓	~✓	N/A	✓	~✓	✓	×	×	✓	✓	×	✓	×	×
Kuwait	83,310	×	-	N/A	✓	✓	✓	×	×	×	×	-	×	×	×
Lebanon	14,690	✓	×	N/A	✓	×	✓	×	×[1,2]	×	×	✓	✓	×	×
Morocco	8,063	✓	×	N/A	✓	✓	✓	✓	×	✓	×	✓	✓	×	✓
Oman	40,240	-	×	N/A	✓	-	-	×[1]	-	✓	×	-	-	×	×
Qatar	128,060	×	✓	N/A	✓	×	✓	✓	×	×	×	✓	✓	×	×
Saudi Arabia	54,770	×	✓	N/A	×	×	✓	×	×	✓	×	✓	✓	✓	×
UAE	74,410	×	~✓	N/A	✓	×	✓	✓	×	✓	✓[2]	✓	✓	✓	×

Note: [1] Primary and secondary data collection and triangulation with multiple sources suggest this criterion is not met.
[2] While it has been mentioned that local decision-makers consider the international implications, it is unclear how this is applied in practice.
[3] Median price.

Key: '✓' = satisfies.
'×' = does not satisfy.
'~✓' = partially satisfies.
'-' = no evidence

Source: LSE interpretation based on primary and secondary data collection and further triangulation with stakeholders. GDP per capita data from World Bank, 2018.

7.2. Issues relating to coverage, reimbursement and procurement in the MENA region

Fragmented and limited reimbursement systems: Many of the countries in the MENA region have fragmented reimbursement systems with many actors involved in the purchasing of medicines, delivery of healthcare, and reimbursements mechanisms. In principle, most countries have comprehensive health insurance coverage; in practice, however, comprehensive health coverage occurs across the GCC countries (for citizens), whereas some of the other study countries have incomplete coverage and a sizeable OOP expense. Most countries in the region rely on a combination of government funding, national health insurance schemes, and OOP spending to fund their healthcare systems. (See Appendix 4 for further information on reimbursement systems in the study countries). Although coverage is claimed to be universal in other countries in the region, the achievement of that goal is placed somewhere in the future. Recently, Egypt enacted legislation which promised to deliver universal coverage by 2030, among other things.

Dominance of tendering in public procurement: tendering is the most prevalent mechanism for the procurement of *off-patent and generic pharmaceuticals*. Tendering is, however, often used in combination with other mechanisms: for off-patent products, these mechanisms include internal reference pricing (Algeria, Morocco), CBA (UAE), and formulary management (Algeria, Lebanon, Saudi Arabia). For generic products, these mechanisms include IRP (Algeria, Lebanon, Morocco) and formulary management (Algeria, Lebanon, Saudi Arabia). Tendering is also widely used for the procurement of *in-patent pharmaceuticals* (Egypt, Jordan, Lebanon, Morocco, Saudi Arabia).

Shortcomings of public procurement systems: The evidence points in the direction of certain inefficiencies in public sector procurement, which can have a knock-on impact on prices achieved, whether these relate to originator or off-patent drugs. First, the study countries do not necessarily procure cheaper, generic pharmaceuticals but more expensive innovative medicines. This is because of a lack of cheaper pharmaceuticals (Saudi Arabia), the lack of procurement of low priced generics (Egypt, Jordan, Kuwait, Lebanon, and the UAE), unavailability of generics due to non-price factors (Egypt, Jordan, Kuwait, Lebanon, and the UAE), or unnecessary reliance on some innovator brands (Kuwait) (BMI, 2016e; Ball et al., 2005; WHO, 2007b). Governments could undertake increased generic public sector procurement where opportunities exist and this could have a favourable impact on prices.

Second, the study countries do not always achieve low prices for procured essential medicines (generics). A WHO comparative report of eight countries in the broader region showed that the public sector in Morocco, Jordan, Lebanon and Kuwait usually procures generics at a higher price than the other study countries[5] (WHO, 2008), while in Kuwait, average public sector procurement prices were reportedly 10% higher than international reference prices (BMI, 2017g)[6]. Nonetheless, not all MENA countries report high public sector procurement prices.[7] In the UAE, lowest priced generics were obtained at a median price ratio (MPR) of 0.68 in public sector procurement (WHO, 2008)[8], while in Egypt, the public sector does not procure originator brands, and procures its lowest price generics at a MPR of 1.07, although some common generics still have steep procurement prices (WHO, 2011, 2011a; WHO, 2008).

Actions taken to mitigate inefficient public sector procurement are limited to ***Jordan*** (where joint/unified procurement was introduced because different public health institutions bought the same pharmaceutical through tenders at different prices, caused shortages and higher pharmaceutical spending) (Al-Abbadi et al., 2009) and to ***Algeria*** (where tender prices are kept confidential).

Reimbursement delays and availability: Reimbursement policies and practices can also affect availability. One example, where this has been shown to be the case was Jordan, where public sector procurement was performed through independent annual tenders issued in the generic name of the pharmaceuticals or therapeutic groups, by four governmental parties (RMS, JUH, MoH, and KAUH) (Al-Abbadi et al., 2009). This mode of procurement may limit pharmaceutical availability for beneficiaries and has been shown to result in increased pharmaceutical expenditure. This is because it can lead to double purchasing whereby the government pays for more than one public health organisation purchasing the same pharmaceutical in the same year at distinct prices (Al-Abbadi et al., 2009). An obvious solution in this context would be joint or unified procurement, which was implemented in the case at hand (Al-Abbadi et al., 2009).

Increased interest in Health Technology Assessment: Health Technology Assessment (HTA) is not used in the MENA countries' reimbursement systems, nor are there independent or quasi-independent institutions tasked with the conduct of HTA

[5] The study also included: Jordan, Kuwait, Lebanon, Pakistan, Sudan, Syria, Tunisia and Yemen. Only Syria procured higher prices for generics.
[6] Other evidence suggests this may even be higher: originator brand prices at 2.69 times the international reference price, and the lowest priced generic prices at 1.39 times the international reference price (52).
[7] The surveys used Management Sciences for Health (MSH) 2003 international reference prices, and WHO/Health Action International methods (WHO, 2008). Public procurement prices were gathered but because retail pharmacies' official price lists were used, there is no guarantee of the price paid by the patient (WHO, 2008).
[8] Expensive originator brands occur at a MPR of 4.97.

(whether this is on the clinical cost effectiveness or the comparative clinical benefit assessment analysis). However, there are trends in legislation and policy across the region where HTA and/or efficiency interests are stated either explicitly (Egypt) or implicitly (Saudi Arabia). In some cases (Egypt, Lebanon), it is increasingly recommended to submit economic analysis (e.g. budget impact) aiming to aid negotiations with manufacturers, particularly on the front of new and expensive innovative products.

Increased use of risk-sharing agreements: Risk-sharing agreements (RSAs) are used very sparingly in the MENA region; some preliminary evidence has been reported for expensive, innovative products for rare diseases (Algeria, Egypt, Lebanon), but it is unclear how these may have been operationalised and whether they qualify as RSAs. Despite current implementation being very novel and preliminary, there is an interest in these agreements. This is true for (a) arrangements around discounts and do not include outcomes-based agreements, and (b) in the scope of their use, as seen in Lebanon, where the implementation of RSAs is limited to a single payer in a multi-payer system. It is also important to note that the legislative frameworks around RSAs is unclear and is thought to be non-existent across the study countries.

ERP and reimbursement: ERP is not used as a reimbursement tool in the study countries. However, in several countries, ERP prices set in the pricing process become the starting point for negotiations or other reimbursement methods (Algeria, Egypt, Lebanon, Morocco) and more often than not, ERP prices are 'transferred' to reimbursement.

Movement towards mandatory generic prescribing: There is a larger effort towards implementing mandatory generic prescribing, currently in place in four study countries (Jordan, Oman, Qatar, and the UAE. The practiced is encouraged in two study countries (Algeria and Lebanon). However, none of the countries has implemented an electronic system to manage generic prescribing practices.

Limited mandatory generic substitution: Generic substitution is not widely required in the MENA region: while most study countries have a generic substitution policy, it has only been made mandatory practice in one country (Jordan). This trend is also linked to the relative lack of compulsion of using generic medicines – where possible – in order to improve affordability and is an area of policy that requires attention by local decision-makers.

7.3. Issues relating to local industrial policies

Across the study countries, there seems to be significantly more support provided to domestic than to foreign manufacturing entities. Domestic manufacturers receive support through taxation/subsidies (Saudi Arabia, Algeria, and Bahrain), registration (Jordan), reimbursement (Bahrain, Egypt, Jordan, Kuwait, Lebanon, Morocco, Qatar, and Saudi Arabia), pricing (Saudi Arabia, UAE, Egypt, and importation (Jordan, Morocco, Oman, and Saudi Arabia). Overall, support for domestic manufacturers is predominantly through pricing and reimbursement policies which discriminate against multinational manufacturers. The most commonly provided support, is public procurement which gives preference, including price advantages, to local manufacturers (Saudi Arabia, Egypt, Jordan, Bahrain, Kuwait, Morocco, Lebanon, Qatar).

On the other hand, foreign manufacturers receive support only through taxation or subsidy incentives (Bahrain, Morocco, Kuwait, Qatar, and Saudi Arabia), which are not necessarily tailored for the pharmaceutical sector but apply generally, and in reimbursement (Algeria), and pricing (Qatar).

7.4. Impact of pricing, reimbursement and procurement policies in the MENA region

As shown in the preceding sections, evidence on and analysis of the impact of pricing, reimbursement and procurement policies in the study countries has been at best patchy, often remains anecdotal and is very frequently confusing because of the presence of two important elements in the MENA region: the first is the incomplete coverage (including prescription drug coverage) by the health care system, which effectively means that in many of the study countries there is a significant out-of-pocket element for health care services and, particularly, pharmaceuticals, while the other is inadequate distinction in the pharmaceutical market between originator medicines and generics and their respective impact. These two elements often lead to unclear or contradictory conclusions. Taking these into consideration, in this section we discuss the available evidence on impact and benchmark against a set of important endpoints, such as the regulatory/pricing system, the availability and affordability of medicines and the international implications of local regulation.

7.4.1. Impact of Pricing Policies (ERP) on Prices in MENA Region

Structure of Pricing/ERP systems: The evidence generally indicates, that ERP and the way it is structured and implemented, delivers "low" pharmaceutical prices in the MENA region by international standards. Primary data collection confirms that ERP results in

"low" prices in ***Algeria, Egypt[9], Lebanon, Qatar,*** and ***Saudi Arabia*** (Primary Evidence: Algeria, Egypt, Lebanon, Qatar, Saudi Arabia, 2018) compared to the basket they are referring to as the price selection is geared towards the lowest in the basket. This is in line with available published evidence from Egypt, Lebanon and Saudi Arabia concerning branded originator products. The ***UAE*** was falling in this category until very recently, but the new pricing guidelines and the stipulations therein, particularly in what concerns the composition of the basket and the price selection (median rather than the lowest in the basket) have changed the outlook for this country, assuming all products will subscribe to this rule (Primary Evidence: UAE, 2018).

In ***Lebanon***, Decision 301/1 caused 872 pharmaceutical prices to decrease on average by 20% (Ammar, 2009)[10] and due to ERP legislation, Lebanon's pharmaceutical prices are among the lowest in the Middle East (BMI, 2017c, 2016c). In ***Egypt***, the impact of Ministerial Decree 499[11] implementing ERP decreased product prices for branded products and international companies' products (Mohamed, 2014; Mohamed and Kreling, 2016; BMI, 2016b)[12]. Finally, ***Saudi Arabia***[13] normally achieves the lowest prices amongst the GCC states based on its basket (Primary Evidence: Saudi Arabia, 2018; BMI, 2017i).

Market-related features: Beyond the design of ERP systems, the features of the market in which ERP is implemented (e.g. population size) also appear to impact in-patent price levels in the MENA region. A larger population size combined with a mandate of lowest price in basket are significant explanatory variables of in-patent pharmaceutical price levels across the study countries and, specifically, in ***Egypt, Jordan, Kuwait, Lebanon, Saudi Arabia, Qatar, and the UAE*** (Kalo et al., 2015)[14]. The referencing of more than

[9] Public price referencing and steep profit margins (30-40%) lead to low CIF for new products.
[10] Decision 301/1 implemented price adjustments based on a price comparison with Saudi Arabia and Jordan. The revised Decision 51/1, caused a pharmaceutical price decrease in the range of 3-15% (Ammar, 2009).
[11] Decree 499/2012 was introduced in June 2012 and effective in October 2012, and superseded Decree 373/2009. The Egyptian Initiative for Personal Rights (EIPR) challenged Decree 373/2009 before the Administrative court claiming this pricing system based on ERP was a threat to Egyptians' health (Wanis, 2015). The decree was suspended but came back into play following appeal by the MoH, until Decree 499/2012 superseded it three years later.
[12] The study (Mohamed and Kreling, 2016) finds local divisions of international companies' products and imported products with price changes, were predominantly branded and higher priced, and they mainly decreased in price. Local divisions of international companies and imports represented 28.5% and 2% of products with price changes respectively (20). Of the local divisions of international companies' products with price changes: they were generally in the higher price category (64.3% were high price, 19.7% were medium price, and 16.1% were low price), 12.5% were generic, and 23% on the EDL. Of the local divisions of international companies' products with price changes, 71.4% decreased in price. The two most common therapeutic classes for local divisions of international companies' products with price changes were cardiovascular products (21.4%) and psychotropic products (23.1%) (20). Furthermore, of the products with price changes, only 4 were imports and these were all high in price, 25% were generic and 50% increased in price.
[13] Its ERP legislation takes the lowest price of 40+ countries, including Turkey, Egypt and Greece, which contributes to the low prices (Primary Evidence: Jordan, 2018). If a lower price is listed in reference countries during the five-yearly review of pharmaceutical product registration submission, the price in Saudi Arabia is lowered (Primary Evidence: Jordan, 2018).
[14] To compare price levels in the seven MENA countries, the study collected the prices in the seven countries of 14 non-pharmaceutical services, and 16 patented pharmaceuticals (Kalo et al., 2015).

five countries is not a significant explanatory variable for in-patent pharmaceutical prices (Kalo et al., 2015). The products included in the ERP system when associated with other policy tools may also impact price levels; in ***Algeria*** pharmaceuticals with generic equivalents are subject to ERP for reimbursement, while patented pharmaceuticals without generic equivalents may be referenced against generics considered to be in the same therapeutic class (therapeutic referencing).

Level of government control: Government control in itself is a necessary but – in itself – not a sufficient condition for reducing prices of pharmaceuticals. Market dynamics can lead to price adjustments in response to action by decision-makers. One such case is ***Lebanon***, where the implementation of a unified medical prescription policy changed the dynamic of branded pharmaceutical dispensing and pricing patterns with some brand pharmaceutical prices were aligned to and occasionally fell below generic prices (Saleh et al, 2017; El-Jardali et al, 2017).

GCC price harmonisation process and race to the bottom: The GCC pharmaceutical price harmonisation process[15] has already led to a substantial downward impact on pharmaceutical price levels in the GCC states, including ***Bahrain*** (BMI, 2017j), ***Oman*** (BMI, 2017e), ***Qatar*** (BMI, 2017i), the ***UAE*** (BMI, 2017h) and ***Kuwait*** (BMI, 2017g). In ***Saudi Arabia***, if the current CIF price for a pharmaceutical is not the lowest among the GCC states during the price harmonisation process, it will lower its price to the same level as the lowest price (Primary Evidence: Saudi Arabia, 2018). Of course, ability to pay across the region varies based on GDP per capita in the GCC members and the GCC pharmaceutical price harmonisation process gives credence to the belief that ERP acts as a cost containment measure with price convergence towards the lowest, irrespective of GCC members' market size, consumption preferences or priorities, and GDP per capita. Based on that and because GCC prices are referenced by other countries in the region (e.g. Egypt), it may be the case that some countries are potentially over-paying for medicines, whereas others are under-paying.

On balance, it appears that ERP reduces the price differential between countries of different economic status, and leads to a narrower price range for innovative pharmaceuticals across the MENA region. Overall, the impact of ERP can be quite distorting as it creates artificial benchmarks, which are not necessarily linked to tangible or robust local assessment systems. As a result, ERP may not be the optimum pricing policy for achieving

[15] The GCC for Drug Registration (GCC-DR) is in the process of applying pharmaceuticals price harmonisation, over four years in Oman, Qatar, Saudi Arabia, Kuwait, Bahrain, and UAE. The process involves aligning the CIF price of all marketed presentations in phases subject to therapy groupings (Kalo et al., 2015).

competitive and appropriate price levels, compared to a more dynamic pricing policy which allows pharmaceuticals to express value in their national context. Despite that, and to the extent ERP continues to be implemented, it is necessary to maintain a confidential net pricing system which will allow competent authorities and manufacturers to negotiate based on the formers' needs.

7.4.2. Pricing Policies and likely Access Barriers and Availability Concerns

A country's pricing policy, its degree of inflexibility and the length of the negotiation process can indirectly impact pharmaceutical availability through influencing the price levels a manufacturer can achieve in that country, thereby impacting their decision to launch and/or withdraw a product in/from a market. Although there is limited quantifiable evidence, the following examples highlight the likely impact of pricing policies' impact on availability.

Pricing policy: If a country's pricing policy leads to prices that are visible and are considered to be too low compared with international standards, manufacturers – if allowed - may withdraw products from a market (if regulation allows it), or, more likely, not launch at all, adversely affecting availability. ERP and using the lowest price in the basket, can cause barriers to access for new and innovative pharmaceuticals through launch delays in ***Algeria*** (Primary Evidence: Algeria, 2018). In Algeria, companies are concerned about a spill-over effect if they concede a price below the lowest price in Europe (Primary Evidence: Algeria, 2018) (see section on International Implications of ERP for further detail). Consequently, there have been time-limited supply shortages for some products, where they are imported in limited volumes and are in monopolistic situation or where there is a limited quantity of manufacturers globally, in which case manufacturers prioritise high-price markets more so than low-cost markets such as Algeria (Primary Evidence: Algeria, 2018).

Pricing system inflexibility: The flexibility of a country's pricing system, whether that is to accommodate external effects such as the exchange rate fluctuations or depreciations, or to consider inflation, can affect pharmaceutical availability, through impacting a manufacturer's decision to remain in a market. We examine this issue, and its corresponding solutions in two examples. Such inflexibility, may result in product withdrawals from the market or delays in launching them. Consequently, highly regulated markets may experience lower pharmaceutical availability than more flexible markets. In ***Algeria***, shortages may be caused in part by the financial challenges some local manufacturers are experiencing in relation to some of their pharmaceuticals since the ex-

factory prices are fixed in local currency (Primary Evidence: Algeria, 2018). In ***Egypt***, there are regular pharmaceutical shortages[16], and only 8,000 of the 13,000 registered products are available (Wanis, 2015)[17] and there have been some shortages for some expensive and high-priority essential pharmaceuticals for around two years (Primary Evidence: Egypt, 2018). These shortages are directly linked to pharmaceutical prices, and the currency devaluation which makes it difficult to import raw materials (Primary Evidence: Egypt, 2018). This is because the pricing scheme does not allow price rises to counteract inflation, nor does it adjust for the E/R and hence the increasing raw material import costs (BMI, 2017b). Since the currency devaluation more recently, distributors of medicines for serious conditions such as cancer, reduce and/or stop imports to avoid loss at resale under the low-price regime (Kholaif and Lohade, 2016). Consequently, vital pharmaceuticals for some critically ill patients are unavailable, such as 48 medicines including anticancer medications (Kholaif and Lohade, 2016).

Protracted negotiation process: pricing schemes can limit pharmaceutical availability through *protracted price negotiations and approval*, which delay market entry or product launches. In ***Jordan***, protracted price negotiations have resulted in delayed market entry for some imported medicines (BMI, 2017, 2016). A study on ***Egypt, Jordan, Kuwait, Lebanon, Saudi Arabia, Qatar and the UAE***, has shown that ERP implementation may reduce timely access to new medicines through delayed market entry, since some of the countries report that prices of some new pharmaceuticals remain unapproved, until reference countries have established their prices (Kalo et al., 2015).[18]

7.4.3. Affordability issues

Evidence on affordability: Pharmaceutical affordability is an issue of varying importance across the MENA region. Pharmaceutical affordability is an issue in Lebanon, UAE, Egypt, and Morocco (Primary Evidence: Lebanon, UAE, Egypt 2018) whereas it is not considered an issue in Algeria or Qatar (Primary Evidence: Algeria, Qatar 2018). In Jordan, there are some affordability issues depending on the therapeutic class (Primary Evidence: Jordan, 2018). Clearly there are many factors influencing or shaping pharmaceutical affordability,

[16] This is contradicted by an earlier 2004 WHO/HAI pricing survey (see WHO, 2001, 2011a for more information). According to a 2004 WHO/HAI pricing survey, public sector availability of originator and lowest priced generic medicines is 100%. One reason provided for 100% pharmaceutical availability is the use of an EDL which is in line with the list of medicines utilised in the survey. Equally, the survey demonstrates 100% private sector availability for originator and generic medicines. However, these figures are calculated using a single point in time. Furthermore, this information is outdated in comparison to more recent evidence provided.
[17] The regular shortage of certain pharmaceuticals can be explained by the fact that often manufacturers which face operating at a loss because of price decisions, produce 1-1 batches of the pharmaceutical annually to safeguard their registration files (Wanis, 2015).
[18] Although at the time the study was conducted, the UAE used a fast track pricing process whereby it would only reference the country of origin, to hasten priority drugs access.

including the overall regulatory (pricing) framework for pharmaceuticals but also the level of coverage and the drug benefit provided by the health care system and the health care system type itself (publicly funded, the extent of OOP payments, etc).

Level of health insurance coverage: In Egypt, Lebanon, and Morocco although prices are somewhat responsible for affordability issues, there are other contributing factors (Primary Evidence: Lebanon, Egypt, 2018), such as the lack of universal health coverage (Primary Evidence: Lebanon, Morocco 2018). In Morocco, there is a significant difference between the prices people pay and what they can afford (BMI, 2017d). This is due to insufficient coverage (BMI, 2017d). In some cases, access and affordability are improved upon by action through alternative channels, whether these relate to activities by NGOs or broader government action on pharmaceutical policy. In Morocco, civil societal actions have improved innovative medicines access to the poorest patients via the Lalla Salma Foundation[19] for the fight against cancer, which signed a memorandum with pharmaceutical manufacturers to enable innovative oncological drug access for poor patients through various public oncology centres (Brahmi et al., 2016). Also, the MoH announced in 2017 that it has approved some generic medicines as part of the National Drug and Pharmaceutical Policy directed at delivering affordable medicines (BMI, 2017d). In other instances, countries have resorted to price cuts in order to improve affordability (e.g. in 2015, the Lebanese government lowered the prices of 30 branded and 60 generic medicines to increase health care access; however, despite the price reductions, many individuals continue struggling to afford medicines (BMI, 2017c, 2016c), but these actions also need to be viewed from the perspective of availability and the likely impact they will have on that particular dimension of access. In Lebanon, most of the medicines for life threatening diseases, including cancers and multiple sclerosis among others, are provided through an independent financing scheme overseen by the MoPH.

Pricing system and middle-income countries (MICs): Even in circumstances where there is sufficient coverage and the drug benefit is considered to be adequate, an inflexible pricing system – particularly one that 'borrows' prices from other settings, without further elaboration or negotiation, may delay or even deter price approval, and consequently, market entry in LICs. In Lebanon and Egypt, regulators/payers did not approve the price of certain priority originator pharmaceuticals in some cases on affordability grounds, i.e. due to potentially large budgetary impact for payers/patients (Kaló et al., 2015), resulting in problems for medicines access in these countries. Other pricing options, such as linking the prices of generic medicines to those of the originator brands (price capping) has been

[19] Foundation Lalla Salma for treatment of cancer targets RAMED patients (Primary Evidence: Morocco, 2018).

found to generate affordability concerns. It has been suggested that Jordan's pricing policy and its application are amongst the reasons its medicines are unaffordable (El-Dahiyat and Curley, 2017; Ibrahim, 2015) in that the pricing system enables local manufacturers to price their pharmaceuticals as high as 80% of the originator price (El-Dahiyat and Curley, 2017). Furthermore, the small Jordanian demand encourages local manufacturers to demand maximum prices, because they rely on the export market which usually requests the country of origin price at negotiation. Additionally, the pricing policy promotes competition only between originators and generics, not between generics, (El-Dahiyat and Curley, 2017; Ibrahim, 2015) and this is an area where policy could change, among others by re-visiting the broader supply chain, including distribution and generic manufacturing and its role and influence.

ERP and affordability: ERP does not definitively impact pharmaceutical affordability in LICs. Despite the preceding evidence showing ERP can reduce affordability in Egypt, a study demonstrates that Decree 499 which includes ERP provisions, succeeded in altering prices with limited impact on affordability (Mohamed, 2014; Mohamed and Kreling, 2016)[20]. The affordability issue in itself is not only related to the pricing method, but is also inexorably linked to the way that medicines are reimbursed and the methods that are used to ensure that reimbursed prices are affordable. If, as appears to be the case in the majority of MENA countries, the ERP is a price that is reimbursed by the countries concerned without further action on reimbursement negotiation, then, unavoidably, questions arise about the extent to which such prices are affordable.

7.4.4. International implications of ERP

Given the nature of ERP, international implications such as spill-over effects in third countries, are to be expected. The evidence on international implications and their impact is presented as three key issues: (a) spill-over impact of ERP to third countries in terms of launch delays; (b) the effect of ERP on third countries in terms of price convergence and the direction of the convergence; and (c) whether the decision-making community is aware of the international implications of ERP, and if so, their response to them. **Table 17** below summarises pricing policies and their international implications.

[20] To assess affordability, the study uses the WHO and HAI method (Mohamed and Kreling, 2016). The cost of treatment for an acute illness (calculated as the cost for seven days) or chronic episode (calculated as the cost for thirty days) is compared with the lowest-paid unskilled government worker's daily wage, to calculate the number of days' wages required to purchase the treatment. Treatments which cost one day's wage and below are deemed affordable.

Table 17: Pricing policies and their international implications: Summary of available evidence

	Launch delays	ERP leads to (downward) price convergence	GCC price harmonisation leads to price convergence	Decision-makers attempt to mitigate international implications of ERP
Algeria	✓	✓	-	×
Bahrain	-	✓	✓	-
Egypt	✓	✓	✓	×
Jordan	✓	✓	✓	-
Kuwait	×	×	✓	-
Lebanon	✓	✓	×	-
Morocco	✓	-	-	×
Oman	-	-	✓	-
Qatar	×	✓	✓	-
Saudi Arabia	×	✓	✓	-
UAE	×	×	✓	×

Key: '✓' = yes / used
'×' = no / not used
'-' = no evidence.
Source: The authors from the literature.

Launch delays: ERP can cause delays in the launch of new medicines in other countries. Evidence shows that ERP may delay new medicines access because some new medicine prices remain unapproved until reference countries have determined their prices (Kalo et al., 2015). Primary data collection confirmed that the average delay for New Chemical Entities launched in Algeria, and Egypt of 11.4 and 8.9 years respectively (Primary Evidence: Algeria, Egypt, 2018). In Algeria, ERP and utilising the lowest price in the basket may partly cause the lengthy delay to market for new and innovative products, since manufacturers are concerned about spill-over effects if they concede a price as low as in Turkey or Greece, or below the lowest price in European countries (Primary Evidence: Algeria, 2018). The perception of Algeria as a low-price market is reducing its market appeal, and therefore companies establish an order of markets in which to enter first, for example as in the cases of Sovaldi and Harvoni (Primary Evidence: Algeria, 2018).

Price convergence: ERP implementation can lead to price convergence across the MENA region. The available evidence shows that ERP policies adopted by the MENA countries lead to innovative pharmaceutical product price convergence. In ***Egypt***, international reference pricing leads to pressure for new product prices to be aligned (Primary Evidence:

Egypt, 2018) irrespective of economic status. Evidence also suggests that ERP decreases the pharmaceutical price differential between countries of different economic status (Kalo et al., 2015). The GCC price harmonisation process is leading to downward price convergence since the price harmonisation process will continue reducing pharmaceutical prices in the broader MENA region as well as in the GCC states (BMI, 2016g). Countries including Egypt, Jordan and Algeria reference GCC countries in their reference pricing systems, leading to additional downward price pressure (BMI, 2016g). Overall, the innovative pharmaceuticals price corridor in the Middle East will be narrowed further and will depend less on countries' economic status (Kalo et al., 2015).

Decision-making community's response to international implications: The decision-making community's awareness and response to the international implications of ERP, differs between countries in the MENA region. In some cases there is awareness of ERP's international implications, but these are not taken into consideration; examples are the ***UAE, Egypt, Morocco, and Jordan*** (Primary Evidence: UAE, Egypt, Morocco, Jordan 2018). In ***Jordan*** decision makers' predominant focus is the achievement of the lowest price, therefore, they are not concerned with ERP's international implications (Primary Evidence: Jordan 2018). In other cases, decision-makers are aware of the international implications of ERP and attempt to mitigate them, as, for example in ***Algeria***. In order to avoid spill-over effects, Algerian decision makers are working to establish the best legal mechanism by which to determine two prices, a list price and a confidential transaction price[21] (Primary Evidence: Algeria, 2018). One way they are doing so can be seen in the way tender prices have been made confidential since 2016 (Primary Evidence: Algeria, 2018).

[21] The confidential transaction price applies primarily to hospital pharmaceuticals, and innovative products in oncology and immunotherapy (Primary Evidence: Algeria, 2018).

8. Policy options – What is the way forward?

By reflecting on the evidence provided in the previous sections, in this section we are exploring a number of policy options for the future. These options first of all reflect on the peculiarities of ERP and how the current system as is implemented in different MENA countries can transition to a more effective tool over the mid- to long-term; second, they also reflect on how the limitations of current systems of coverage and reimbursement can be overcome and what the requirements are for the establishment of more formalised arrangements around value assessment that will rely more on evidence than on borrowing prices from other settings.

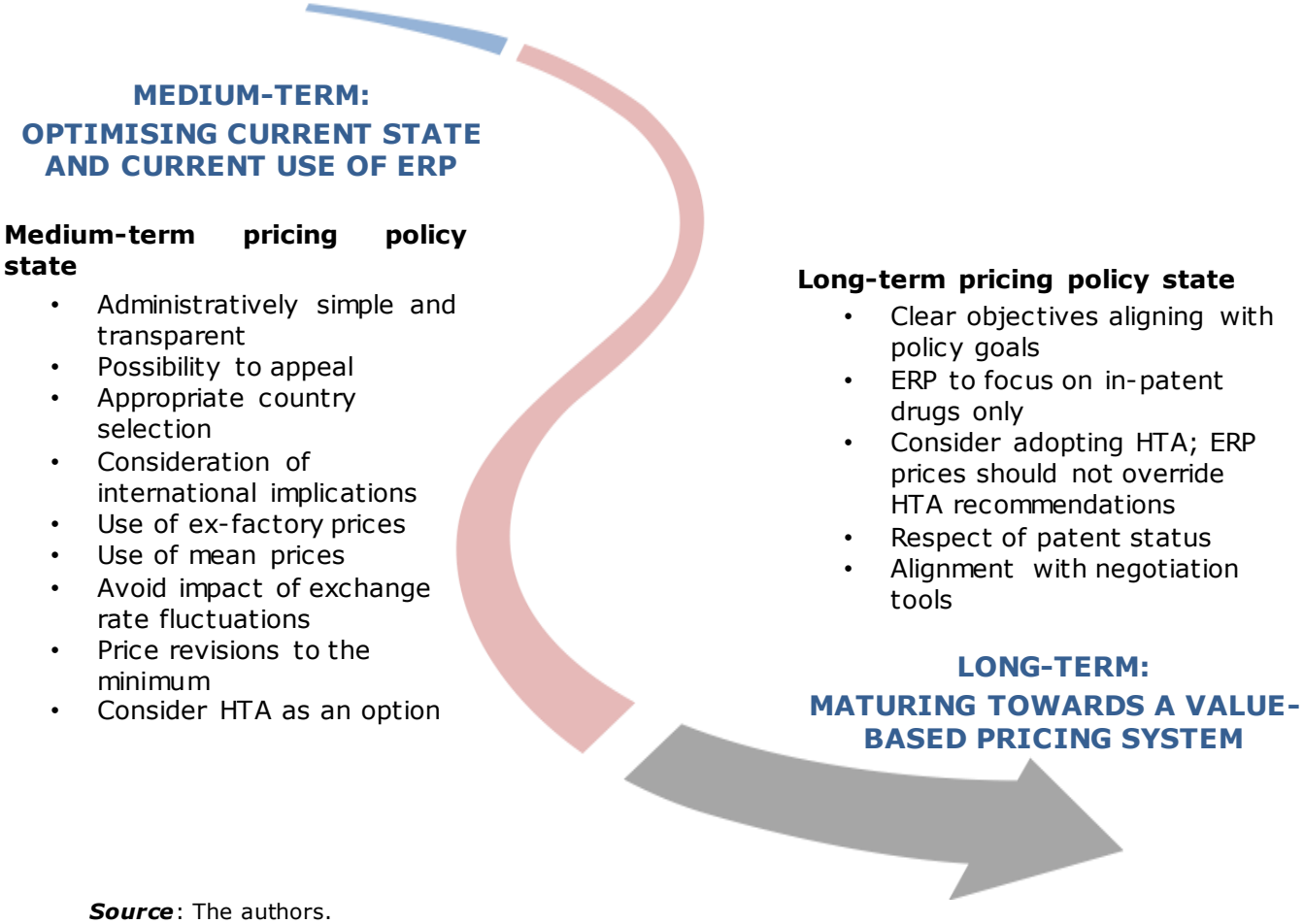
8.1. How can the current pricing system become more effective or efficient and what steps are needed for that?

The first question we are addressing in the context of policy options for the future relates to the current pricing system and the way it can become more effective or efficient and what are the requirements for this. The analysis using the framework of the 14 best practice principles in the MENA countries is quite revealing and, in practice, may suggest a number of ways forward. These have both a medium-term and a long-term perspective. Figure 1 shows the pathway towards an ERP system that is based on best practices and distinguishes between medium- and long-term interventions and perspectives. We discuss both of these in the sections that follow.

8.1.1. Interventions in the medium-term

MENA decision-makers can optimise ERP systems in the medium-term by intervening constructively and refining certain elements that are further away from best practice. Priority should be given to the following elements: (a) improvements in administrative simplicity, (b) the existence of robust appeals mechanisms, (c) the selection of reference countries in the sample, (d) recognising and taking into account the international implications of ERP, (e) using publicly available ex-factory prices to shape list prices, (f) using mean (or at least median) prices rather than lowest, (g) avoiding the exploitation of exchange rate fluctuations, (h) keeping price revisions to a minimum and (i) work towards the adoption of HTA (Figure 1). These are explored in the following paragraphs along with options for the MENA countries.

Figure 1: Medium- and long-term Pricing Policy Strategy in the MENA region



Source: The authors.

Administrative simplicity and transparency: Options for MENA countries

Ensuring administrative simplicity and transparency is important for several reasons. First, systems with these characteristics are easier to manage, which means that fewer resources will be required in order to establish and maintain them. Second, these features allow all relevant stakeholders to anticipate pricing decisions. This is also important for suppliers of pharmaceuticals in terms of obtaining clarity in each market they operate in. Uncertainty surrounding pricing mechanisms may cause suppliers to delay or even prevent entry into certain countries. In addition, price negotiations will likely be more straightforward if all parties concerned clearly understand the country's pricing mechanisms, especially if these prices are strictly enforced. When deviations from the

typical pricing procedures occur, the rationale should be documented and made publicly available. Finally, simple, transparent systems are less prone to invisible transactions and are easier to audit in order to promote efficiency.

The interpretation of administrative simplicity rests on two key features of ERP: the first is the size of the basket of reference countries and the second is the frequency of price revisions. Large baskets and frequent price revisions increase significantly the costs of compliance and the overall running costs of the system. Both (a large basket of countries and frequent price revisions) are features of the current systems being implemented in the MENA countries.

Consequently, the current state of affairs cannot be argued to promote administrative simplicity, despite the fact that that the processes in question are clear and transparent and enshrined into legislation. In this context and assuming MENA countries are willing to move in the direction of an administratively simple and transparent EPR framework, the following options are proposed:

- First, to reduce the size of the basket of reference countries significantly and as well as reduce the frequency of price revisions to the minimum possible, the latter meaning at most once every two years or each time there is a re-registration, whichever is longer.
- Second, ERP applies with a small basket of reference countries at launch only, therefore, it is only conducted once, and the size of the basket declines to a manageable size (between 5-7 countries). This option assumes that, whereas ERP retains its role as a pricing system, emphasis will be placed into a value assessment system that ultimately determines reimbursement levels. In order to move to such a system, it will be important to have in place alternative options for reimbursement and value assessment, which enable reimbursement to be based on robust and objective criteria.

Box 1 below summarises these options.

Box 1: Administrative simplicity and transparency - Options for MENA countries

In order to make the system of ERP administratively simple as well as increase its transparency further, the available options are as follows:

- Retain ERP and reduce the size of the basket of reference countries to meaningful levels and reduce the frequency of price revisions.
- Retain ERP with a small basket of reference countries (between 5-7) at launch only.

Appeals processes: Options for MENA countries

In general, regulators should develop a process and provide opportunities for stakeholders to appeal pricing decisions made explicitly using ERP. Allowing for appeals is essential, given the inherent uncertainty in prices developed via any ERP system. For example, referenced prices will not reflect actual transaction prices, and referenced countries often use unknown methods of arriving at a given price. In addition, the appeals process may illuminate issues with the ERP system's design or management. It will also allow extenuating circumstances to be presented and considered. If the appeals process results in a price change, the reasons for this change should be documented, in order to maintain transparency. Further, the process for appealing decisions and the timing of such appeals should be straightforward, and the requirements of this process must be made readily available to stakeholders during the review process. Finally, appeal timeframes should be kept finite, and timelines should be understood and adhered to by all parties. Not doing so could result in protracted pricing negotiations at the expense of ensuring access.

Based on the above, it is recommended that stakeholders should have the ability to appeal to the appropriate competent authority the results of the pricing process in the current setting and, where this exists, it is recommended that this continues in the future. If it does not exist, it is highly recommended that the ability to appeal decisions is enshrined into legislation. Appeals panels comprising relevant stakeholders, examines all cases within a timely fashion. 'Timely' in this context means between 3 and 4 weeks at most. This option is summarised in Box 2 below.

Box 2: Appeals process: Options for MENA countries

Stakeholders should be able to appeal regulator decisions in a timely fashion, typically between 3 and 4 weeks in order to avoid delays in access.

Selection of reference countries: Options for MENA countries

Selecting reference countries with a similar economic status and health system objectives increases the likelihood of arriving at appropriate price levels, which align with other healthcare decisions made within the country. Referencing countries that are of a lower economic status or have unusual economic conditions should be avoided. Demanding the same price in lower-priced markets as in higher income markets could cause innovative pharmaceuticals to become prohibitively expensive for lower income countries.

In addition, heavily referencing lower-income countries could lead pharmaceutical companies to delay launches in those countries because of the fear of lower prices in these countries and the element of 'cross-infection' to third countries that use the former as reference. At times, lower-income countries reference prices in higher-income countries, where more sophisticated methods are used for determining value and pricing, such as economic analyses associated with HTA. If this practice is followed, prices can be adjusted, for example, using purchasing power parity – denominated (PPP) exchange rates, or through a per capita income adjustment indicator (wealth adjustment). A final consideration in the context of selecting reference countries is the size of the basket. Smaller baskets are in principle preferred to larger baskets, not least because of the high administrative cost associated with large baskets and in the absence of a single, validated source of data that can be available across all basket countries. Additionally, the objective of a reasonable and affordable price within a small basket can be maintained by ensuring a wealth adjustment if it is perceived that some basket countries have an income higher than the country referencing them.

The current baskets that most MENA countries use lead to an overtly laborious, time-consuming and administratively heavy process of price calculation and re-calculation; this process may be prone to errors, which are often attributed to formulation and/or dosage differences across countries, leading to delays in producing an accurate price list and creating imbalances on the market. Consequently, it is proposed that the basket of reference countries that MENA countries use should be reduced to a much smaller basket in order to ensure greater transparency, flexibility, responsiveness, accountability and stability.

Based on these criteria, MENA countries have a number of options, which would make the process of price setting simpler, easier and more transparent, without contributing to increases in cost, as follows: first, country baskets could contain all countries with similar levels of GDP and possibly similar in market size; second, stability can be further safeguarded by introducing a notion of fixed exchange rates (see relevant point below); and, third, if the resulting basket includes countries with higher income levels than the MENA country in question, a wealth adjustment based on GDP per capita differential (at PPP levels) between the country in question and the MENA country, could be applied in order to ensure that the latter will not be overpaying relative to its per capita income. Box 3 below summarises the above options.

Box 3: Selection of reference countries: Options for MENA countries

1. Basket countries could be selected on the basis of similar GDP levels and/or market sizes;
2. Fixed exchange rate regimes could be promoted up to a point;
3. Wealth adjustments could be used in order to ensure that MENA countries do not overpay relative to (some of) the basket countries.

International implications of ERP implementation should be considered

In the preceding section(s) we have highlighted that the wide use of ERP often has a number of unintended consequences internationally, which may directly or indirectly affect members of the broader stakeholder community. Worldwide decreases in drug prices may lead to decreases in R&D of new products. Additionally, a downward convergence is likely to lead to launch delays or, even, withdrawals with concomitant implications for access. Consequently, the value of pharmaceutical innovation to the healthcare system should somehow be considered and reflected in drug prices. This perspective requires that systems consider the international implications of their pricing policies. There are also concerns that ERP may cause access disparities through price increases, launch sequencing and non-entry into certain markets.

There is a significant amount of cross-referencing across the MENA region and this includes the GCC price harmonisation process, which are also referenced elsewhere in the region. The prospect of very low prices in the region is likely to lead manufacturers to not launch new products or launch them with significant delays and towards the end of their patent protection period, once price-setting elsewhere has taken place by using next-best reference country options.

Based on the above, it is therefore recommended that: first, list price levels in MENA countries should remain at a level that manufacturers are still encouraged to launch effective products in these markets rather than bypassing them fearing of spill-over effects elsewhere. Second, if the current basket configuration changes to include a different basket of countries, wealth adjustment by GDP would still ensure that list prices in MENA countries are affordable. And, third, even if list prices are thought to be higher than what might otherwise be expected, the negotiation of list prices to produce reimbursement prices will ensure that MENA countries achieve significant savings on their pharmaceutical budget without placing undue pressure on list prices. Box 4 below summarises the points raised above.

Box 4: International implications of ERP implementation – Options for MENA countries

1. List price levels should remain at a level that manufacturers are still encouraged to launch effective products in MENA countries;
2. Considering a smaller and more flexible basket of reference countries, wealth adjustment can be used to ensure that list prices in MENA countries are affordable based on each country's income;
3. The reimbursement system and the negotiation of confidential reimbursement prices should be used as the main lever to produce savings on the pharmaceutical budget by reducing the cost of new medicines, whilst leaving list prices unaffected.

Use of publicly available ex-factory prices

Ex-factory prices are most reflective of actual transaction prices. Other prices, such as the retail price, incorporate additional costs, which vary across countries (e.g. wholesaler costs, pharmacy service fees and taxes) and are subject to national regulatory practices. Using publicly available sources to locate price information is necessary because it encourages transparency, though this information is not always available for all countries.

A number of issues are relevant and important in this context for MENA decision-makers. First, MENA decision-makers should be aware that there may be circumstances where the available price from a basket country is the wholesale and retail price. While this may be the exception rather than the rule, it will require MENA decision-makers to arrive at ex-factory prices by using the appropriate wholesale and/or retail mark ups and/or VAT rates. Caution should be exercised while using specific mark ups as these may vary according to the product price (regressive mark ups) both at wholesale and the retail level. Given the complexity that wholesale and/or retail prices present in terms of the amount of information required, it is recommended to altogether exclude such countries and only accept in the basket countries that only report ex-factory prices.

Second, many countries publish routinely (and very often online) the list prices of prescription drugs in their country. Often, however, there may be alternative sources of price data, for example, referring to prescription drugs for use in hospitals, or price data related to tenders. MENA decision-makers should exercise caution when attempting to use publicly available tender price data from basket countries for the domestic retail market, as the two are completely different markets.

Third, increasingly, countries negotiate discounts with manufacturers, off the list price. In the vast majority of cases these discounts are confidential (and, therefore, are not reported), but there may be circumstances where such prices can become available, in which case they can be used. Overall, publicly available data sources should be used to

extract ex-factory prices from basket countries. Box 5 below summarises the above recommendations.

Box 5: Use of publicly available ex-factory prices - Options for MENA countries

1. Altogether exclude countries reporting wholesale and/or retail prices and only accept in the basket countries that report ex-factory prices;
2. Ensure that list prices extracted from other countries are relevant to the subject matter of external price referencing, i.e. setting list price primarily for the retail market;
3. Publicly available data sources should be used to extract ex-factory prices from basket countries; for transparency purposes, discounted prices can be taken as reference prices if they are published and are verifiable.

Choice of mean price based on ERP principles

Currently, most ERP systems in MENA region use the lowest price of referenced countries when developing a national target or list price; this is particularly the case in the GCC rules and the knock-on effects elsewhere in the region. Assuming that reference country selection is based on similar economic status and health system objectives, using the minimum price is generally not appropriate, since countries with the lowest prices may have unusual public health or economic circumstances, which could justify such a price. Therefore, an average price rule should form the basis of ERP systems. The median can be used if outliers are a concern.

If prices are not available in all reference countries, delays should be avoided, and price setting should proceed based on available information in order to strike a balance between basket size, administrative simplicity and desirable outcome. Doing so increases the likelihood of selecting a reasonable price while ensuring information availability. However, the number of countries referenced will be constrained by the need to select economically similar countries as well as maintaining an administratively simple system. Again, decision makers should also consider incorporating additional methods of selecting target prices.

A number of considerations are relevant for the MENA country context based on the above discussion. First, by selecting the mean, rather than the lowest price in any basket of countries to set its own target prices, a given MENA country avoids pressure from manufacturers about the spill-over effects of that price to other settings. Second, in any basket of countries, even if incomes are similar, there is a variation in prices. The selection of the target price will largely depend on how the target price is used in the process of reimbursement. If target prices are the point of departure for reimbursement negotiations,

the mean is a desirable outcome. Third, basket country selection including countries with (much) higher incomes, may require some wealth adjustment in order to arrive at 'affordable' prices for given MENA countries. Box 6 below summarises the above points.

Box 6: Choice of price based on ERP principles – Options for MENA countries

1. By selecting the mean or median, rather than the lowest price, MENA countries avoid pressure from manufacturers about the spill-over effects of that price to other settings;
2. If target prices are the point of departure for reimbursement negotiations, the mean is probably a desirable outcome;
3. Country selection based on similar GDP per capita levels will imply that selecting the mean can also be an optimal result. Country selection including countries with (much) higher incomes, may require wealth adjustment in order to arrive at 'affordable' prices for some MENA countries.

Dealing with exchange rate volatility

Exchange rates can vary dramatically over time, so using an exchange rate at a single time point may result in unstable or perverse price estimates. Therefore, we recommend employing techniques to decrease the impact of this volatility on the estimated price, such as using a moving average of the exchange rate.

Another issue with exchange rates is that they do not completely adjust for the purchasing power of a given currency, which can vary even when referencing countries of a similar economic status. To address this issue, countries could consider using purchasing power parity (PPP) exchange rates, though calculation of these rates and selection of the basket of goods with relevance to pharmaceutical products is less straightforward than for traditional exchange rates. An alternative would be to adjust prices to per capita wealth levels in the actual country compared with its comparators.

ERP baskets contain currencies from many different countries, which are often subject to fluctuation. Considering that exchange rate fluctuations can have dramatic effects on prices, which are caused by external factors, the options that MENA decision-makers would have to address this issue are as follows: first, if countries with different currencies are still included in the ERP basket, then exchange rate fluctuations can be mitigated by enabling a moving average of spot or annual average exchange rates to be taken, for example, the average of the past 1 or 2 years. This way, abrupt appreciations or depreciations based on external factors can be accounted for and the moving average approach can have a smoothening effect on the exchange rate used. Second, purchasing power parity (PPP) exchange rates can be used and these will reflect individual country purchasing powers. This is probably an optimal solution, but requires caution because of

PPP availabilities and the representativeness of pharmaceutical PPPs. Third, prices derived from the first or the second option above, or the current methodology using current exchange rates, could be adjusted by the wealth levels of the respective reference countries. This is tantamount to using a wealth adjustment to ERP explored earlier in this section. Box 7 outlines the available options discussed above.

Box 7: Dealing with exchange rate fluctuations – Options for MENA countries

MENA countries could consider one of the following options in order to address the adverse event of currency fluctuations:

1. If different currencies are included, consider for these an exchange rate which will be based on moving average principles
2. Use PPP-based exchange rates
3. Adjust prices by the level of wealth, proxied by GDP at PPP level

Consider HTA as an option

While HTA significance is highlighted in the policy circles of many countries of MENA, its formal adoption (actual and potential) is practically non-existent as of autumn 2018 (only examples of mentioning HTA are in Egypt and Saudi Arabia). Even in Egypt and Saudi Arabia, the mechanisms of its use are still unclear. It is unlikely that ERP will cease to be the main determinant of pharmaceutical pricing in the MENA region. However, HTA can supplement decisions in many scenarios. Before doing so, however, it would be important for countries wishing to implement it, to reflect on the infrastructure needed, (human resources, physical resources, data collection), in order to increase national capacities in conducting technology evaluations, understand the use of value assessment methods and calibrate these according to national priorities that also support innovation and inward investment. Finally, as value is multi-dimensional, additional dimensions of value should also be considered in such a model; these can be societal (e.g. family or caregiver burden), innovation-related (e.g. ease of access, dynamic impact), or related to the disease (e.g. burden of disease, severity).

8.1.2. Interventions in the long-term

The long-term interventions by MENA decision-makers in the context of improving their ERP systems relate to (a) the clear (re-)alignment of ERP objectives with health system objectives, (b) the focus of ERP on in-patent products only, (c) the fact that ERP should not override HTA or alternative approaches (e.g. VBP), (d) the respect of patent status and (e) the alignment of ERP-based prices with other tools used when negotiating

reimbursement (Figure 1). These principles and the associated options are discussed further in the paragraphs that follow.

Objectives of EPR and alignment with health system objectives

Outlining the objectives and scope is an important first step in designing an ERP system. Objectives and scope should be reassessed on a routine basis. Some objectives are clearly universal, such as the desire to achieve fair prices for new health technologies. However, the goals of the overall health system should be considered as well. For example, health systems often value promoting future health through innovation and ensuring fairness and equal access to healthcare interventions.

All objectives should be considered so that the ERP system functions cohesively within the health system and does not focus too narrowly or becomes short-termist in nature. Alignment of the EPR system with the objectives and values should be reviewed periodically, and legislation should be kept current. In addition, mechanisms should be developed for monitoring in order to ensure that target prices are selected and used in accordance with the guiding objectives.

As part of this, MENA countries could consider developing methods of determining value, such as therapeutic value assessment and/or economic analyses as part of a health technology assessment (HTA) process. Countries should be encouraged to establish prices using alternative methods more explicitly, particularly those related to value assessment. While not all countries may have capacity to do this on their own, ERP in those settings could evolve into a system that takes into account countries that derive prices via value assessment methods.

The pricing system for prescription medicines – and, in particular, on-patent medicines - in MENA countries needs to be viewed upon in the context of how it fits in the overall system of financing medicines. It is imperative to ensure that a number of principles are highlighted and met; for example, principles such as simplicity, stability, predictability and cost efficiency, to name a few, are important, not only for those who run the system, but also for those who are subjected to it. These principles in the majority of cases need to be enshrined into legislation. Additionally, it is important that the role and objectives of ERP are highlighted in relation to the overall pricing and reimbursement system. For example, in the process of reimbursement there may be a re-definition of objectives, or the establishment of processes over and above those postulated by ERP. In this case, a re-calibration of the role of ERP needs to be considered also from a legislative perspective and ensure the separation of pricing from reimbursement.

As a result, a series of options arise for MENA countries, which are **not** mutually exclusive; indeed, they can be perceived as recommendations as they align with good practice internationally: First, the objectives of the ERP system need to be clearly spelled out and be binding for stakeholders; such principles include simplicity, stability, predictability, transparency and cost efficiency. Second, the role of ERP within the entire system of pricing and reimbursement of pharmaceutical products needs to be defined, making sure that if the need arises for adaptation, the processes are available for this purpose. And, third, re-calibrate the role of EPR according to changes in the system of reimbursement. If an explicit system of value assessment is established in individual MENA countries, this may unavoidably require changes in the way ERP functions; this may also include its breadth, coverage, as well as frequency of price revisions. Box 8 below summarises the options discussed above.

Box 8: Objectives of ERP - Options for MENA countries

1. ERP needs to have clear objectives enshrined into legislation, e.g. simplicity, stability, predictability, transparency and cost efficiency.
2. The role of ERP in relation to other tools in the wider pricing and reimbursement function needs to be defined.
3. ERP may require re-calibration depending on changes in the overall system of pricing and reimbursement for example, the introduction of explicit value assessment techniques.

Focus of the EPR system on in-patent products

Without external controls, the relative lack of competitive forces for newly launched, on-patent pharmaceutical products can result in high or/and unaffordable prices. With this in mind, ERP is most appropriately applied to on-patent medications, which prevents problems from applying ERP for the same product/molecule by different manufacturers. Off-patent medications are naturally subject to greater competitive forces, which result in driving prices down. For this to work, however, it needs to be safeguarded that health care systems in MENA countries have mechanisms in place that guarantee the quality of off-patent medicines. In addition, there are other mechanisms available for directly or indirectly regulating prices of off-patent medications, such as price capping or internal price referencing, the latter being used extensively to set a price ceiling on reimbursement. Referencing prices of therapeutically similar off-patent medications within a country has a greater probability of resulting in prices that reflect their therapeutic value. MENA countries should consider using other methods to price and reimburse off-patent medicines. Although price capping is used in many MENA countries, primary data collection has shown

that the remit of ERP can include off-patent medications. It also protects products that although are off-patent, the do not have generic alternatives on the market. Subjecting off-patent medicines to ERP is rather counter-intuitive and potentially leads to higher prices for those medicines. Importantly, genericised medicines are subject to national rules and measures and EPR may offer limited insights into pricing of such products.

A number of options are, therefore, available in the MENA context: the first option, centers around the continuation of ERP alongside price reductions, but local decision-makers need to ensure that over time there will be a process of *gradual* de-linking from ERP principles for off-patent drugs in this space. The second, promotes the abolition of ERP for off-patent drugs and the implementation of a sensible price reduction once patent expires, on the understanding that this price reduction is sufficient to capitalise on the potential offered by patent-expired drugs/generics and could be set at -50 to -60% of the pre-patent expiry price. The third option, centers around the abolition of ERP for off-patent drugs and the implementation of a sensible price reduction once patent expires, to be coupled with an element of dynamic competition, linking the number of entrants on the product/molecule market to further price declines. Several of the countries in the region are already implementing this option and it appears that it could be generalised across the region. The fourth option, is to abolish ERP for off-patent drugs and implement a system of price reductions to be coupled with tenders in outpatient/inpatient markets. Tenders often result in very dramatic effects, particularly in out-patient segments. Caution needs to be exercised in this context, because the pursuit of the lowest possible price, particularly in single-insurance/payer systems, may have dramatic effects on competition and how the market functions, therefore it is important to define their reach carefully, ensuring that at best, they can serve a proportion of the market rather than serve as the main/only method of supplying generics. Box 9 outlines the options discussed above.

Box 9: Focus of ERP on in-patent products - Options for MENA countries

1. Continue with the current mix of ERP with price reductions, but ensure that over time there will be a process of gradual de-linking from ERP principles for off-patent drugs in this space.
2. Move away completely from ERP principles and implement a significant one-off price reduction post-patent expiry.
3. Move away completely from ERP principles and implement a considerable one-off price reduction post-patent expiry, coupled with elements of dynamic competition, for sequential entry.
4. Move away completely from EPR principles and consider a combination of sufficient reductions post-patent expiry with tenders in out- and in-patient markets.

ERP and other methods used to determine reimbursement

Several countries utilize ERP as an adjunct to explicit methods of value assessment, such as formal HTA or cost-effectiveness analysis. In principle, we would encourage using multiple approaches. However, some approaches, such as HTA and value-based pricing systems, have a stronger theoretical underpinning, in that they directly consider the overall value of a pharmaceutical product to a population in order to make coverage decisions. By contrast, ERP relies on prices set in other countries, the latter using unknown pricing mechanisms and methodologies. Therefore, ERP-based prices should not override those developed via other more robust evidence-based approaches, if they disagree. Further, final prices should align with conclusions regarding the value of each product to the population. Overall, countries might expect to pay more for products providing greater added value, even if ERP results contradict this. This is important to consider because the groups conducting value assessments are often separate and apart from those ultimately making the pricing decisions, so results may not be integrated appropriately. South Korea, Taiwan and Brazil are current examples.

Based on the above, MENA countries have a number of options concerning other methods of price setting, also linked to the process of determining coverage and reimbursement: First, if prices are selected from settings that use HTA methods or other explicit value assessment methods, ERP should be used as a guide only to price setting and, depending on the strengthening of reimbursement procedures, it could act as a means of informing final decision-making rather than being the key tool for this process. Second, MENA decision-makers could include prices from HTA-based settings in order to inform local pricing decisions. And, third, considering changes in pricing and reimbursement legislation, the role of ERP in MENA countries could evolve to an advisory role based on a refined (and smaller) basket of countries. In this case both countries that follow ERP principles and countries following HTA or similar to HTA principles can be considered for inclusion into the basket. Box 10 outlines the options discussed above.

Box 10: ERP and other methods to determine reimbursement - Options for MENA countries

1. Include countries that use HTA but do not override their conclusion(s) in favour of a lower price
2. Include in basket countries that use HTA, but with similar health care systems and economic status
3. Consider both HTA and EPR countries, but the pricing function becomes advisory and, therefore, less important in the process of pricing and reimbursement.

Respect patent status

When determining target or list prices for on-patent products, whose patents may have expired in one or more reference countries, referring to prices of off-patent medications within the reference countries should be avoided. Patents are usually territorial, which often means that the length of patent protection period remaining may be different in different jurisdictions, even if these belong to the same geographical or/and economic area, such as the European Union. Differential patent protection periods may mean that in some circumstances patents may expire elsewhere first than in a given country in the MENA region, in which case the settings where patents have expired will witness generic competition and – possibly – a price reduction to the originator price. This scenario may mean that the product which is still under patent in a MENA country, may be subject to undue pressure from cheaper generics that are available in other countries where the patent for this product has expired. It is incorrect to subject the patent-protected product price to generic price competition from generics available in other settings. Box 11 summarises the discussion on this important point.

Box 11: Respecting patent status – Option for MENA countries

Expiry of the patent in the domestic market is a pre-condition for subjecting the price of the originator product to generic price competition from other settings (as well as price competition from domestic generics).

Alignment of ERP-based prices with other tools, including RSAs and value assessment

Many countries utilize price setting through ERP as an adjunct to other methods of value determination and risk management, and, consequently, its relative importance in defining list prices varies. When negotiating reimbursement, insurers sometimes enter into managed entry agreements, wherein they agree with a manufacturer to share in the financial risk of introducing a new pharmaceutical agent into a given market. These agreements are confidential in nature and can a take a number of forms, such as price-volume agreements, coverage with evidence development or outcome guarantees. Countries entering into these arrangements will need to consider how the prices developed using ERP align with such agreements. For example, a country establishing an outcome guarantee agreement, by which they only pay for those patients achieving a pre-specified outcome, could have a higher list price than countries without such an agreement.

It is proposed that over the medium-term the ERP system in MENA countries will be transformed into a tool that assists in price-setting and that these list prices will subsequently be used in negotiations with manufacturers when individual products come

to the countries in the MENA region. In this context, price-fixing at entry and subsequent re-pricing will be used as the starting point of negotiations with manufacturers about reimbursement. Reimbursed prices will be confidential.

In this context, and assuming a given MENA country has developed the capacity and ability to negotiate on the basis of RSAs, including the implementation of outcomes-based risk-sharing agreements, list prices at entry will remain important, whereas the role of re-pricing will remain important in order to ensure that list prices are in line with developments elsewhere in its basket, but the relevance of ERP and the basket for setting reimbursement prices will be at best marginal because a process of negotiation will substitute for that. However, re-pricing may be important for those who pay out-of-pocket and therefore, it is recommended that it takes place, but that its frequency declines to once every two years or every time there is a re-registration, whichever is the longer of the two. Box 12 summarises the above discussion on options.

Box 12: Alignment of ERP with other tools – Options for MENA countries

1. List prices are set at launch through the process of ERP; list prices inform the process of reimbursement and will form the basis of negotiation between the appropriate authority and manufacturers to set reimbursement levels; It should be expected that negotiations will lead to prices which are favourable for national payers on condition that these remain confidential;
2. Tools such as RSA and value assessment, through some form of HTA, can be used to inform negotiations;
3. The role of re-pricing in informing reimbursement will – in the majority of cases – be marginal as reimbursement will be based on negotiation rather than a process of re-pricing in order to achieve price reductions over time. If re-pricing is to take place, this should be done once every 2-3 years.

8.2. Transitioning from ERP to VBP

8.2.1. The philosophy of ERP in the context of pharmaceutical policy and to reimbursement

The key objective of ERP currently is to serve as a cost minimisation tool in MENA countries by benchmarking against the lowest list prices from inherently diverse and large baskets. This objective cannot be met as list prices for may or most new products are no longer representative of net or transaction prices in most countries that MENA countries are referencing, due to risk sharing agreements (RSAs), confidential discounting and negotiations between pharmaceutical companies and competent authorities. Consequently, where ERP is used, its fundamental objective has shifted from a cost

minimization tool to a tool that guides negotiations for affordable prices in the reference countries. As such, ERP is a supplement to a range of tools that are used to arrive at affordability, including an explicit value assessment process and the implementation of RSAs. As such, ERP should in principle be the first stage point for negotiations regarding the reimbursability of new products and their inclusion of new products into national benefits' catalogues by enabling the collection of prices from other settings at launch only. MENA countries can continue to implement ERP in the future as well as strive to adhere as much as possible to the best practice principles outlined in the previous section, but safeguard affordability not by resorting to the lowest price in extensive ERP baskets, but by implementing competent negotiation strategies and value assessment methods. To the extent ERP continues to be implemented, it is necessary to maintain a confidential net pricing system which will allow competent authorities and manufacturers to negotiate based on the formers' needs.

Box 13: The role of ERP in the context of pharmaceutical policy

1. ERP is a supplement to a range of tools that are used to arrive at affordability, including an explicit value assessment process and the implementation of RSAs.
2. ERP should in principle be the first stage for negotiations regarding the admission of new products into national benefits' catalogues by enabling the collection of prices from other settings at launch only.

8.2.2. Dealing with innovative and niche products

ERP typically accounts for all new products, including innovative and new products. As the difference between list prices and net prices can be significant particularly for new, innovative and, often, niche products, it would be desirable to commence the process of pricing these products through ERP means. Subsequently, if a separate pathway of negotiation and value assessment has been set up for certain products, it would be desirable to exclude these products from inclusion into ERP updates. This is in line with evidence from many other settings. By creating a separate pathway for innovative and niche products, where a negotiated approach is the preferred course of action, the original list price, achieved through ERP, remains as is (and does not damage the interests of manufacturers overseas), while negotiated prices is likely to be beneficial for health insurers and health systems. There is some patchy evidence suggesting that these practices are beginning to take shape in certain MENA countries (for example, in Algeria, tender prices are kept confidential, while there is a process of negotiation in Egypt in some cases), but these need to be transformed into a systematic process across the region.

Box 14: ERP and innovative/niche products

1. If a separate pathway of negotiation and value assessment has been set up for certain products, it would be desirable to exclude these products from inclusion into ERP updates.

8.2.3. Requirements for the transition from an ERP to a VBP system

Countries in the MENA region have been implementing ERP for several years now, but, over time, it has become obvious that ERP in itself poses significant limitations to early access. In itself, ERP is also limited because it is increasingly associated with fictitious list prices in many (if not most of) the settings MENA countries are using as reference. It has become clear, therefore, that ERP is one of the steps needed to arrive at affordable prices. Even countries that have traditionally relied on ERP to determine prices in their territory and reimbursement rates, are increasingly using ERP as one of the (less important) criteria to achieve their goal.

Over the past 15 years, there has been a gradual shift in many countries from ERP to (a) the establishment of robust criteria for value assessment based on clinical and/or economic grounds, (b) a form of HTA, (c) the consideration of additional criteria beyond costs and effects, which capture the importance of the local context and local data such as burden of disease, incidence, prevalence and severity, (d) the use of negotiation principles to arrive at reasonable and affordable prices and (e) the more extensive use of risk sharing principles to inform local coverage decisions. Important country examples in this context and in the MENA region's geographic vicinity are Spain (where ERP's importance has declined significantly over the past decade in favour of comparative clinical benefit assessment), Italy (completely departed from the principle of average European price to implement HTA, negotiation and extensive risk-sharing), Poland (abandoned ERP and using HTA with a fixed threshold to inform pricing and coverage decisions), Belgium (abandoned ERP in favour of a direct negotiation model based on clinical value assessment and extensive risk sharing), and, more recently, Greece (where the establishment of HTA and direct negotiation with risk sharing will become the dominant model in the future). Outside Europe, important is the experience of Brazil and South Korea in the same vein, while countries such as Turkey are using some kind of HTA and have alternative mechanisms to deal with novel and expensive therapies in a way different than what ERP principles postulate.

The transition of the above countries to more formalised models of value assessment has been made possible through investment in three key areas: the **first** is significant

investment in institution-building, such that there are new competent authorities and institutions to address the challenges of modern value assessment; the **second**, is significant investment in human capital and development of capabilities that are necessary to address the above challenges; and, the **third** relates to data generation processes in order to ensure that whatever decisions are made, can be made on the basis of robust and validated evidence. To an extent, the focus on institutions and human capital determines the roadmap that needs to be followed; evidence from the above settings suggest that transitioning from one model to another cannot be made overnight but that the long-term benefits for local health care systems can be significant, esp. in the context of universal health insurance coverage.

Box 15: Transitioning from an ERP to a VBP system

1. International evidence suggests the transition from ERP to (a) the establishment of robust criteria for value assessment based on clinical and/or economic grounds, (b) a form of HTA, (c) the consideration of additional criteria beyond costs and effects, which capture the importance of the local context and local data such as burden of disease, incidence, prevalence and severity, (d) the use of negotiation principles to arrive at reasonable and affordable prices and (e) the more extensive use of risk sharing principles to inform local coverage decisions;
2. Transitioning towards a more explicit system of value assessment requires (a) institution-building to address practical challenges in value assessment, (b) investment in human capital, and (c) data generation processes to support evidence-based decision-making.

8.2.4. Is there a role for HTA in value assessment in MENA countries?

HTA can play the role of a catalyst in some key MENA markets. The implementation of HTA has so far escaped the MENA region, but there are clear signs that HTA and value assessment are likely to be implemented in some form in countries such as Egypt and Saudi Arabia over the mid- to log-term. Clearly, HTA can offer significant advantages, but is also associated with considerable limitations. Local decision-makers need to be very clear about their objectives, how HTA fulfils these and how it is linked to other tools currently in operation. Before even considering HTA adoption, a ***set of prior actions*** are essential to consider and endorse. First, interested countries should think how it will be incorporated in their decision-making processes, including the interaction with other policy tools, such as ERP. Second, any decision to adopt HTA should be followed by investment in human and physical infrastructure as well as data systems to support its implementation; third, a period of learning is also desirable in this context. Fourth, if HTA is established, it needs to be separated from the registration process and should not impact

registration based on efficacy and safety. Fifth, the principles of HTA should ultimately be applied across a wide range of medical interventions, rather than medicines only. And, finally, the implementation of HTA principles, requires a gradual shift in policy-making towards an environment which is more transparent, collaborative, consultative and is supportive of innovation and investment.

Overall, HTA plays a major role in evidence-based decision-making. Agreement on best practices is important because HTA is increasingly a fundamental part of the way organisations decide on which health technologies they will reimburse. In this context, MENA countries have many options concerning (a) the type of system they can implement and (b) the type of model based on which value assessment will take place.

With regards to the ***type of HTA system***, there are several options in place, which also constitute stages or a roadmap in the adoption and gradual implementation of HTA in the region. The first policy option/stage advocates that HTA is not an explicit process or function in MENA country health care decision-making, but comparative clinical benefit or cost-effectiveness evidence from other settings will be taken into account when considering coverage decisions. Such evidence can be leveraged from available recommendations in other settings. The role of HTA evidence in this context is purely advisory and will contribute to decision-making, albeit in an implicit manner.

The second option/stage promotes capacity-building in and use of HTA by tasking existing institutional stakeholders to develop capacity and share the responsibilities in HTA. Based on this, all new in-patent products as well as line extensions will undergo clinical benefit assessment and will have their budget impact assessed, in addition to an appraisal of cost-effectiveness evidence, the latter only if the ability exists to conduct such analysis locally. Of these, a subset should undergo negotiation for inclusion or not into the benefits catalogue (positive list).

The third option/stage promotes the establishment of an independent HTA agency or institute, which will conduct HTAs based on the principles of "summary evaluation approach". Accordingly, an independent HTA agency/institute will adopt a "*summary evaluation approach*" for all new (in-patent and line extension) products and once HTA experience and capacity have been built the remit of technologies appraised can be expanded to include medical devices and other health care technologies. Selection criteria for negotiation remain the same as in the previous option and will include budgetary, epidemiological, clinical and, possibly, cost-effectiveness.

Finally, the fourth option/stage, favours the establishment of an independent HTA agency or institute based on the principles of a "consultative approach". Accordingly, an independent HTA agency/institute will adopt a "*consultative evaluation approach*", whilst

also considering expanding the remit of the technologies to include medical devices and other health care technologies. If a consultative model is adopted, then a small number of technologies can be evaluated in any given year and selection criteria for these will include budgetary, epidemiological, clinical and, possibly, cost-effectiveness; the same technologies will undergo negotiation for inclusion into the benefits catalogue (positive list). This is probably a long-term option for the majority of countries in the region and will require significant investment in infrastructure as well as adherence to a number of principles such as transparency, predictability and clear role definition.

With regards to the ***model of value assessment***, there are three specific options available: (a) the clinical and cost-effectiveness model, the (b) comparative clinical benefit assessment model and the (c) value-based pricing model. The first uses economic evidence in addition to comparative clinical benefit, the second relies on ranking new interventions based on comparative efficacy/clinical benefit and making the pricing decision the subject of negotiation between government/insurance organisations and manufacturers, while the third option takes explicitly into consideration additional dimensions of value beyond effects and/or costs, such as disease severity, burden of disease, treatment innovativeness, equity considerations, etc. The choice of model is largely dependent on local preferences but also on the type of system that will ultimately be proposed for the settings concerned.

Of course, there are limitations to be overcome in those settings in the MENA region that aspire to implement HTA in the (near) future, and the roadmap is likely to be long; such limitations include, among others, lack of expertise and critical mass, no infrastructure in terms of established organisations and human resources, and broader infrastructure issues, such as the existence or not of a unified reimbursement system in a or broader considerations, e.g. those relating to the stance on clinical trials. Finally, there is a significant number of important details that need to be resolved, including the type of evidence requirements, the guidelines for submission, how assessments and appraisals are performed, what data informs these and whether this data is available in the local context, what constitutes evidence, whether stakeholders are consulted, how recommendations are made and whether they are binding, and how they are implemented.

Box 16: Is there a role for HTA in value assessment?

1. Before even considering HTA adoption, a set of prior actions are needed in order to prepare the ground.
2. Interested countries should think how it will be incorporated in their decision-making processes, including the interaction with other policy tools, such as ERP;
3. A decision to adopt HTA should be followed by investment in human and physical infrastructure as well as data systems to support its implementation; a period of learning is also desirable;
4. If HTA is established, it needs to be separated from the registration process and should not impact registration based on efficacy and safety;
5. The principles of HTA should ultimately be applied across a wide range of medical interventions, rather than medicines only.
6. The implementation of HTA principles, requires a gradual shift in policy-making towards an environment which is more transparent, collaborative, consultative and is supportive of innovation and investment.
7. Interested countries should carefully consider all available options around an HTA system and select one that satisfies their interests before deciding to adopt one;
8. Interested countries should carefully consider all available options around an HTA model, before deciding to adopt one.

8.2.5. Re-thinking universal coverage and reimbursement

Universal health insurance coverage (esp. in terms of services and level of coverage) varies significantly in the MENA region and ranges from 30% - 88%. Populous countries such as Egypt and Morocco have incomplete health insurance coverage and a significant part of pharmaceutical expenditure is paid for out of pocket. Coverage is often very fragmented with significant inequities among different population segments. Elsewhere (e.g. UAE or Saudi Arabia), where coverage of most key services has been good and free of charge for citizens, decision makers realise that a formalisation of the benefits package and the award of the same eligibility rights across different segments of the population requires significant attention, investment and policy intervention.

As such, the goal of universal health insurance coverage (and its implications for the pharmaceutical market) will most likely need to be the focus of policy attention over the next decade or so. Unavoidably, this impacts pharmaceutical reimbursement. The transition from fragmented reimbursement systems in individual countries, based on employment status or type of employment (e.g. government employees or military personnel), to a unitary system with the same principles across all citizens is desirable on equity, efficiency and effectiveness grounds. It will also require significant attention, investment as well as adherence to strict budgetary and efficiency principles.

Undoubtedly, this will have implications for all components of the pharmaceutical value chain all the way from the top end of the market, where the focus is the value assessment of new and innovative treatments and their incorporation into the benefits catalogue in a timely fashion, to the lower end of the market, where there needs to be a more robust and consistent generics policy, both from a supply-side (pricing and price setting) and a demand-side (prescribing, dispensing, cost-sharing) perspective. A sound framework that ensures the quality of generic medicines is an absolute pre-requisite in this context. Beyond generating 'unitary' or single reimbursement systems, national pharmaceutical policies will need to address the issue of financing and its sustainability, a balanced industrial policy, the regulation of the distribution chain, the strengthening of regulatory standards in certain aspects of the pharmaceutical value chain, and the assessment of policy interventions.

Box 17: Re-thinking universal coverage and reimbursement

1. It would be highly desirable to give due consideration to improving coverage sustainably and reducing the OOP cost of health care, including medicines, to the population; having a single coverage or reimbursement system could be one way forward;
2. In the broader context of health care reform, national pharmaceutical policies will need to address the issue of financing and its sustainability, a balanced industrial policy, the regulation of the distribution chain, and the strengthening of regulatory standards in certain aspects of the pharmaceutical value chain, among others.

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Appendix 1: Literature Review Strategy and Results

An extensive literature review was conducted to evaluate all available peer-reviewed and grey literature available on pricing and reimbursement policies in the eleven study countries.

Peer-reviewed literature search strategy

In terms of reviewing the published available evidence, MEDLINE (through PubMed resource) and were searched for peer review literature using a search strategy for English articles published from 1 January 2000 until the time of the start date of the review, 31 January 2018. ProQuest, Web of Science and EBSCOhost (EconLit+CINAHL) were also searched. The team developed a tailor-made key word strategy which reviewed documents published in English. The key words for our search strategy were selected in an iterative manner, so that the number of literature returned was satisfactory in size and large enough to provide comprehensive and robust insights. The key words/search terms for the peer-reviewed literature were as follows:

1) "Price Regulation" *OR* "Pharmaceutical Regulation" *OR* "Regulation" OR "Price legislation" *OR* "Price legislations" OR "Price controls" *OR* "Price control" *OR* "Pharmaceutical Policy" *OR* "Policy" *OR* "Pricing" *OR* "Pricing Guidelines" *OR* "External Reference Pricing" *OR* "External Price Referencing" *OR* "International Price Comparisons" *OR* "International Reference Pricing" *OR* "International Price Referencing" *OR* "Price Harmonization" OR "Price Unification" *OR* "Unified Pricing" *OR* "Reimbursement" *OR* "Coverage" OR "Reference Pricing" *OR* "Price Referencing" *OR* "Tender" *OR* "Tendering" *OR* "Procurement" *OR* "Value Based Pricing" *OR* "VBP" *OR* "Internal Reference Pricing " *OR* "Internal Price Referencing" *AND*
2) "Drug" *OR* "drugs" *OR* "medicine" *OR* "medicines" *OR* "pharmaceutical" OR "pharmaceuticals" *OR* "generics" *AND*
3) "Middle East" *OR* "North Africa" *OR* "GCC" *OR* "Gulf Cooperation Council" *OR* "Algeria" *OR* "Egypt" OR "Morocco" *OR* "Lebanon" *OR* "Jordan" *OR* "Saudi Arabia" *OR* "Kuwait" *OR* "United Arab Emirates" *OR* "UAE" *OR* "Qatar" *OR* "Bahrain" *OR* "Oman"

Grey literature and other sources

The project team also reviewed grey literature and other sources to identify further information on our predetermined endpoints in the study countries. The keywords used for the grey literature search were as follows:

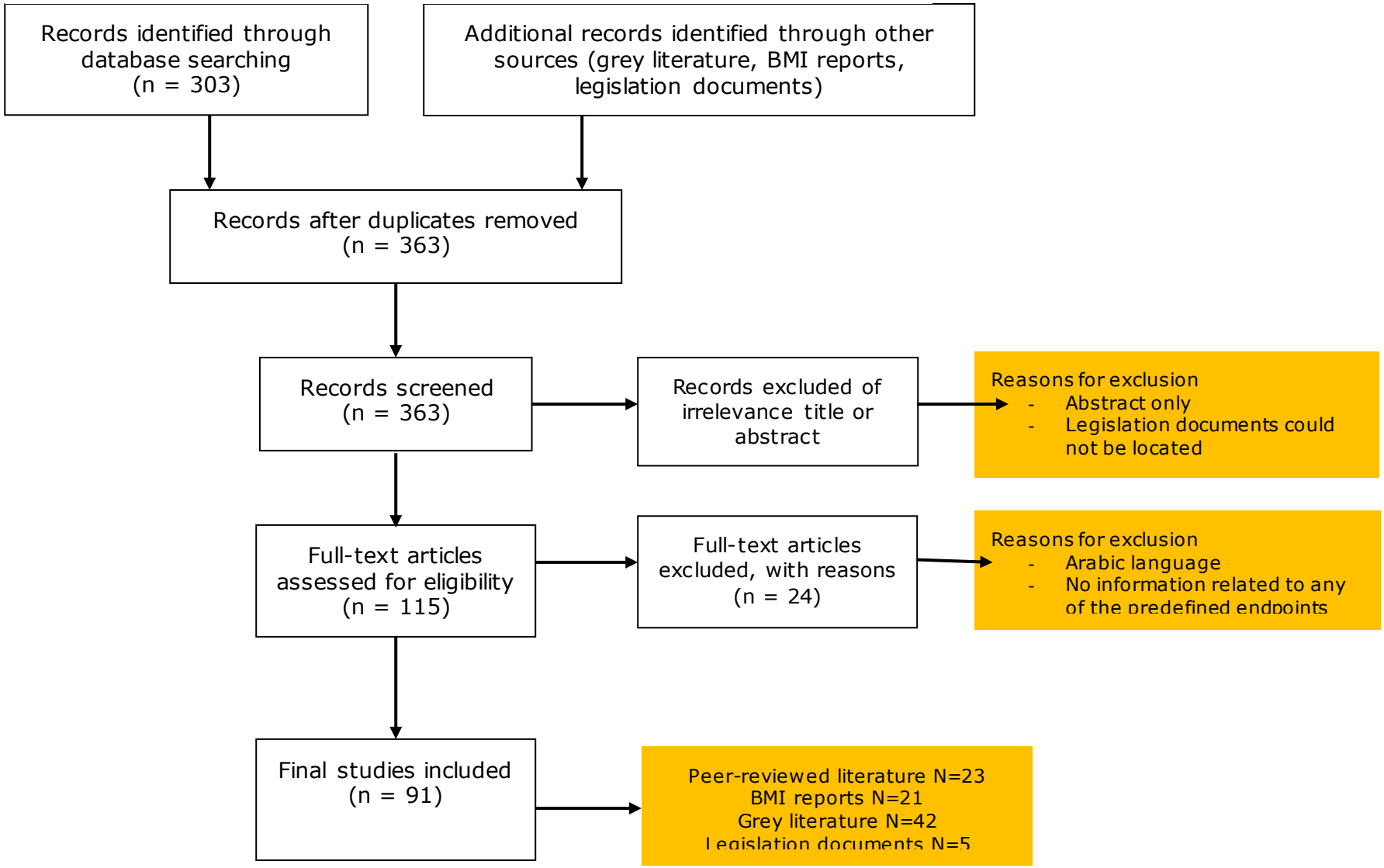
"Price" *OR* "Pricing" OR "Reference" *OR* "Referencing" *OR* "Reimbursement" *OR* "Coverage" *OR* "Tender" *OR* "Tendering" *OR* "Procurement" *OR* "Generic" *OR* "Access" *OR* "Shortage" *OR* "Affordability" *OR* "Manufacturer" *OR* "Tax" *OR* "Discount" *OR* "Prescribing".

The grey literature was much more extensive than the peer-reviewed literature to address this, and therefore the research team focused on the following specific reputable sources:

- MoH and regulatory authority websites in the countries of interest, focusing on Laws and Decrees
- WHO: http://www.emro.who.int/countries.html and http://www.afro.who.int/
- World Bank: http://www.worldbank.org/en/country/gcc and http://www.worldbank.org/en/region/mena
- Business Monitor International (BMI) Consulting reports, focusing on regional and country-specific reports (2017-2018)

The inclusion and exclusion process is outlined in **Figure 2** below. The initial results included 303 peer-reviewed articles and 60 additional documents from grey literature and other sources. After duplicate records were removed, article titles and their abstracts were assessed for the relevance of their content. Subsequently, 115 full-text articles were read, from which were excluded because a) they were in Arabic; and b) they contained irrelevant information. In the end, 91 studies were read and reviewed for incorporation into our report.

Figure 2: Flowchart of the SLR relating to the peer-reviewed literature only



Appendix 2: Interview Discussion Guide

External Reference Pricing & Pharmaceutical Regulation Survey

Questionnaire for key experts in the Middle East and North Africa Region

PROJECT DESCRIPTION

This is a project led by the London School of Economics aiming to map the current Pricing and Reimbursement policies, regulation and legislation in the Middle East – North Africa region and to study external price referencing (EPR) systems, their modalities and implementation across the region as well as its interaction with other pharmaceutical policies and interventions.

Glossary

Cost-effectiveness pricing: The product is priced according to the relationship between its clinical effectiveness, meaning how effective is in comparison to the current standard of care, and its cost-effectiveness in terms of value for money it provides.

Cost-Plus Pricing: A cost-based method for setting the prices of goods and services, whereby the direct material and labor costs, along with the direct and indirect overhead costs of a product, are added to a percentage mark-up in order to derive the price that payers will pay. Direct costs involve costs of all raw materials used that rise in proportion to increased production, while overhead costs referring to all other fixed and sunk costs involved in the production process.

External Reference Pricing (ERP): The practice of using the price(s) of a medicine in one or several countries in order to derive a benchmark or reference price for the purpose of setting or negotiating the price of the product in a given country.

Free Pricing: The manufacturer can price their pharmaceuticals at any price they want.

Internal reference pricing: IRP consists of clustering drugs according to some equivalence criteria and defining a reference price for each cluster, particularly when patents have expired. Clustering can include or exclude patented drugs. If a medicine is priced above the reference price, usually the difference between the price of the medicine and the reference price should be paid by the patient either out-of-pocket or through his/her private health insurance.

Molecular reference pricing: Medicines with the same active substance (ATC-level 5) are grouped to define the reference price.

Therapeutic reference pricing: All drugs that are used to treat a particular condition or medicines that have a comparable therapeutic effect (ATC-level 3) are grouped to define the reference price.

Managed competition in combination with molecular reference pricing: This combines molecular reference pricing and a price cut for additional entrants with the same active substance.

Price capping (X% of the price of the originator before loss of exclusivity (LoE)): The pharmaceutical, usually off patent originator or generic, is priced as a percentage of the price of the originator. For example, the generic to first enter the market will be priced at 60% of the branded product/originator price.

Profit Controls: Prices of pharmaceuticals are indirectly controlled through profit controls to the manufacturer defined as return on capital employed or return on sales. Therefore, the manufacturer can

price the product freely but they should comply with the controls imposed by the payers to the manufacturer's profits.

Risk Sharing Agreement (RSA): Formal arrangement between payers and manufacturers with the aim of sharing the financial risk due to uncertainty surrounding the introduction of new technologies. These agreements can take different forms, including price-volume agreements (PVAs), outcome guarantee, coverage with evidence development (CED), and disease management programmes.

Value Based Pricing: The price that ensures that the expected health benefits of a new technology exceed the health predicted to be displaced elsewhere in the National Health Service, due to their additional cost.

London School of Economics and Political Science

External Reference Pricing & Pharmaceutical Regulation Survey

Questionnaire for key experts in the Middle East and North Africa Region

Introduction

This is a project led by the London School of Economics aiming to map the current Pricing and Reimbursement policies, regulation and legislation in the Middle East – North Africa region and to study external price referencing (EPR) systems, their modalities and implementation across the region as well as its interaction with other pharmaceutical policies and interventions.

Confidentiality

All data obtained from participants will be kept strictly confidential and will only be reported in an aggregate format. All questionnaires will be stored securely, and no one other than the research team will have access to them.

Questions about this Research

If you have questions regarding this study, you may contact the research team (Victoria Tzouma; Email: v.tzouma@lse.ac.uk and Anna-Maria Fontrier; Email: A.Fontrier@lse.ac.uk).

Glossary and list of abbreviations

A glossary and a list of abbreviations are provided in order to define and clarify any terms used in the survey that are not immediately familiar to you.

Acknowledgement

Financial support by PhRMA Middle East & Africa is gratefully acknowledged.

Section 1: Pricing Policies and Price Setting

1. Which country are you completing this survey for?

……

2. What are the objectives of the health care system in your country? (Please tick all that apply).

	Short Term (1-2 years)	Long Term (>5 years)
A. Universal Health Coverage		
B. Cost-Containment		
C. Timely access to essential therapies, including pharmaceuticals		
D. Improvements in equity/reduce inequities		
E. Improvements in efficiency and value for money		
F. Maximisation of health gain		
G. Fast access to innovative treatments		
H. Encouragement of Research and Development		
I. Other, please specify		

3. Are the above objectives reflected explicitly in pharmaceutical policy in your country?

A. Yes
B. No

Please provide any additional information

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……
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…….

4. Which of the policies below are implemented for pricing of in-patent pharmaceuticals in your country? Please tick all that apply.

A. Cost-Plus Pricing
B. Profit Controls
C. Free Pricing
D. External Reference Pricing (ERP)
E. Value Based Pricing
F. Cost-effectiveness pricing
G. Other, please specify

5. Which of the policies below are implemented for pricing of off-patent originator pharmaceuticals in your country? Please tick all that apply.

A. Cost-Plus Pricing
B. Profit Controls
C. Free Pricing
D. External Reference Pricing (ERP)
E. Value Based Pricing
F. Cost- effectiveness pricing
G. Price capping (X% of the price of the originator before loss of exclusivity (LoE))
H. Other, please specify

_____

Option G: Please explain the modality in each case:

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6. Which of the policies below are implemented for pricing of generic pharmaceuticals in your country? Please tick all that apply.

A. Cost-Plus Pricing
B. Profit Controls
C. Free Pricing
D. External Reference Pricing (ERP)
E. Value Based Pricing
F. Cost-effectiveness pricing
G. Price capping (X% of the price of the originator before LoE)
H. Other, please specify

_____

Option G: Please explain the modality in each case:

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7. Do the above policies capture the private sector or are they only meant for the public sector?

A. They are meant for the entire market, whether public sector or private sector or out-of-pocket
B. They are meant for the public sector market

If you answered B in the above question, please specifty what pricing methods are used in the private or out-of-pocket sector:

_____

_____

_____

8. Is there a different pricing policy for locally-manufactured and imported pharmaceuticals?

A. YES
B. NO

If yes, please specify in the box below the pricing policy used for locally-manufactured and for imported pharmaceuticals respectively?

Pricing policy for locally-manufactured pharmaceuticals:

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……

Pricing policy for imported pharmaceuticals:

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……
……

9. Is ERP used in pricing and/or reimbursement decisions? Please tick all that apply

A. Pricing decisions only

B. Pricing decisions are informing (but not determining) reimbursement decisions

C. Pricing decisions are explicitly determining reimbursement decisions

Please provide any additional information if you answered B or C:

_____
_____

10. When was external reference pricing first introduced in your country? (Please specify year)

_____

11. Which authority is responsible for setting pharmaceutical prices in your country? (Please tick all that apply)

A. Ministry of Health

B. Ministry of Trade

C. Ministry of Industry

D. Other competent authority, please specify

_____

Please provide any additional information

……

12. Are there (or have there been) any other stakeholders involved in the design of external reference pricing policy? (Please tick all that apply)

A. This is (or has been) the competent authority's responsibility only

B. External stakeholders are involved, e.g. industry, academia, patient groups, etc.

Please provide any additional information if you answered B

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13. How big is the basket of countries used as reference to set external reference pricing? (Please tick one)

A. Up to 5 countries

B. Up to 12 countries

C. Up to 24 countries

D. More than 25 countries

Please specify the actual number of countries in your basket: _____

14. Has the reference basket changed over the last 5 years? Please tick all that apply.

A. No changes
B. Some changes have been made to the number of countries
C. Some changes have been made to the choice of countries

If you answered B, what changes have been made and when was the last time your country reviewed the basket?

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15. Please name the countries in your basket and provide any additional information (e.g. if some countries are of higher importance than others, etc.)

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16. What criteria are used to select basket countries? (Please tick all that apply)

A. Geographical proximity
B. Comparable GDP levels
C. Country of origin of the product
D. Socioeconomic factors
E. A combination of the above, please specify:
   _____
F. Other criteria, please specify:
   _____

Please provide any additional information

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17. If the patent in one or more of the basket countries has expired and this product, as a result, is available as a generic, then:

A. Your country continues to take the off-patent originator brand price to inform your basket

B. Your country takes the cheaper product/generic product price to inform your basket if its price is available

Please provide any additional information

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18. What is the role of ERP in the final price determination? (Please tick all that apply)

A. Leads to the final list price in your country
B. Is used as a starting point for negotiations about the final list price
C. Is one of several criteria for list price setting
D. Reflects transaction (net) prices
E. Prices derived through ERP are the starting point for negotiations regarding reimbursement.

Please provide any additional information

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19. Are the ERP objectives clearly stated in legislation?

A. Yes

B. No

Please provide any additional information

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20. Please comment on the arrangements regarding product launch and price setting in your country (Please tick all that apply)

A. MA is not granted without agreement on price
B. Following Marketing Authorisation (MA), a new product must be launched with agreement on price
C. Following MA, a new product can be launched and price setting can take place subsequently
D. A new product can be launched without marketing authorisation or agreement on price

Please provide any additional information

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21. If manufacturers disagree with decisions made by competent authorities, are there a any provisions for an appeal?

A. Yes

B. No

If you answered Yes, please provide any additional information about the timelines for the appeals process and settlement of disputes/disagreements

……
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…….

22. Which price is used to inform pricing decisions/negotiations? (Please tick all that apply)

A. Ex-factory price in reference countries
B. CIF price in reference countries
C. Wholesale price in reference countries
D. Retail price in reference countries

Please provide any additional information

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23. What are the sources of information you use to identify and validate prices that inform ERP in your country?

A. The manufacturer that submits the application
B. Public information sources from reference countries (eg. Governmental websites in reference countries)
C. Private sources of information
   Please specify type of source: _____
D. Access to confidential pricing information
   Please specify type of source: _____
E. A combination of the above

Please provide any additional information

.....
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.....
.....

24. How is the reference price calculated in your country?

A. Using the average price in the basket
B. Using the median price in the basket
C. Using the lowest price in the basket
D. Using average price in the basket and making wealth adjustments based in differences in GDP per capita between our country and the basket countries
E. Using the average of the "n" lowest prices in the basket;
   If you ticked E, please specify what "n" is: _____

F. Other, please specify:
   _____

25. How frequently are prices revised in your country? (Please tick all that apply)

A. Every four years
B. Every five years
C. Two years after initial registration
D. When price changes in the country of origin
E. When price changes in key basket countries
F. Other, please specify:
_____

Please provide any additional information that may be relevant:

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.....
.....
.....

26. When prices in different currencies are taken into consideration, what exchange rates are used to translate prices from foreign currencies to your country's currency? (Please tick all that apply)

A. Moving average (please specify how many months or years in the box below) .....
.....
B. Current exchange rate
C. Fixed exchange rate (please describe the arrangements in the box below)
D. Using single currency countries only (e.g. Euro) and taking the current exchange rate
E. Other, please specify:
_____

Please provide any additional information if you answered A or C

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.....

Section 2: Reimbursement and Coverage Decisions

27. Do you know who are the payers of pharmaceuticals in your country? (Please tick all that apply)

A. Government
    a. Full cover ……
    b. Partial cover ……
B. National Health Insurance
    a. Full cover ……..
    b. Partial cover …….
C. Private Health Insurance
    a. Full cover ……
    b. Partial cover ……..
D. Out of pocket (patient pays the full amount of the pharmaceutical

28. What type of pharmaceuticals are most likely to be covered by the health Insurance?

A. All
B. Some
C. Other, please specify_____

29. What type of pharmaceuticals are most likely to be covered by the government?

A. All
B. Some
C. Other, please specify_____

30. Which of the policies below are implemented for reimbursement/procurement of in-patent pharmaceuticals in your country? Please tick all that apply.

A. External Reference Pricing (ERP)
B. Tendering
C. Managed Entry/ Risk Sharing Agreements
D. Health Technology Assessment (HTA)
E. Formulary management
F. Comparative clinical benefit assessment
G. Other, please specify
_____

31. Which of the policies below are implemented for reimbursement/procurement of off-patent pharmaceuticals in your country? Please tick all that apply.

A. Internal Reference Pricing (IRP). If yes, what type?
    a. Molecular reference pricing
    b. Therapeutic reference pricing
    c. Managed competition in combination with molecular reference pricing
B. External Reference Pricing (ERP)
C. Tendering
D. Managed Entry/ Risk Sharing Agreements
E. Health Technology Assessment (HTA)
F. Formulary management
G. Comparative clinical benefit assessment
H. Bio-equivalence
I. Other, please specify

_____

32. Which of the policies below are implemented for reimbursement/procurement of generic pharmaceuticals in your country? Please tick all that apply.

A. Internal Reference Pricing (IRP)
    a. Molecular reference pricing
    b. Therapeutic reference pricing
    c. Managed competition in combination with molecular reference pricing
B. External Reference Pricing (ERP)
C. Tendering
D. Managed Entry/ Risk Sharing Agreements
E. Health Technology Assessment (HTA)
F. Formulary management
G. Bio-equivalence
H. Other, please specify

_____

33. Is there a link between ERP and any other supply- or demand-side regulations (e.g. other pricing policies such as cost-plus pricing, rate-of-return, price caps, or reimbursement policies such as internal reference pricing or or formulary management, etc.) in the pharmaceutical sector?

A. Yes
B. No

If Yes, please expand in the box below.

……
……
……
…….

34. How does ERP align with other policies/practices used when arranging coverage?

A. ERP Is used as a starting point for negotiations about the final list price
B. ERP is used as the starting point for negotiations regarding the reimbursement price.
C. The reference price is de facto the reimbursement price
D. ERP is used as one of several criteria for determining the reimbursed price
If you tocked this box, what other criteria are used in determining the reimbursed price? Please specify:
_____
E. ERP reflects transaction prices
F. ERP reflects list price only rather than transaction prices

Please provide any additional information in the box below

……
……
……
…….

35. Are Risk Sharing Agreements (RSAs) used in your country to determine coverage price?

A. Yes
B. No

36. If you answered Yes in the previous question, when were RSAs first introduced in your country/ institution? (please insert year in the space below)

……
……

……
……

37. What is the relationship between ERP and RSAs? Please expand in the space below.

……
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……
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……
….

Section 3: Evidence of ERP impact within and across countries

38. To your knowledge does ERP lead to or is able to secure low prices? (Please tick all that apply)

A. ERP leads to and secures low prices in our country

B. ERP does not lead to or secure low prices in our country

C. There is mixed evidence on the ability of ERP to secure low prices in our country

Please provide any additional information or perspective

……
……
……

39. Is there any evidence of drug product shortages in your country?

A. Yes
B. No

40. If you answered YES in the previous question, is there any reason to believe that product shortage issues may be due to pharmaceutical prices?

A. Yes
B. No

Please provide any additional information or perspective and include product class, if possible

……
……
……
……

41. Are you aware which countries in the region use the pharmaceutical prices in your country as reference for calculating the prices in their country?

A. Yes
B. No

If you answered Yes, please provide any additional information or perspective

……
……
……
…….

42. Are you aware of any barriers to access for new and innovative pharmaceuticals due to ERP policy in your country?

A. Yes
B. No

43. If you answered yes to the previous question, could you please provide a few concrete examples?

Please elaborate your examples in the box below

……
……
……
…….

44. Do you believe that affordability of pharmaceuticals is an issue in your country?

A. Yes
B. No

If you answerd A, please elaborate on the available evidence.

……
……
……
…….

45. If there is evidence of affordability problems what patient types are likely to be affected? (Please tick all that apply).

A. Patients covered by the Government
B. Patients covered by Health Insurance
C. Patients who pay out of pocket

46. In your opinion, for patients facing affordability issues and have to pay out of pocket for their pharmaceuticals, is affordability a problem for:

A. All pharmaceuticals
B. Some pharmaceuticals
    a. Originator/Branded products
    b. Generics
    c. Other, please specify (e.g. biologics, specialty drugs, etc):
    _____

47. If you answered B or C in the previous question, to what extent do you think are prices responsible for this?

A. Definitely responsible
B. Somewhat responsible, but there are other factors at play
C. Not at all responsible.

Please provide additional information or perspective if necessary.

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.....

48. Does your country have any of the following policies for pharmaceutical companies? (Please tick all that apply).

A. Provides tax breaks/exemptions to foreign manufacturers
B. Provides tax breaks/exemptions to local manufacturers
C. Provides tax breaks/exemptions to all manufacturers, foreign or local
D. Promotes inward investment in R&D
E. Supports local manufacturing through differential tariffs for APIs vs finished products
F. Supports local manufacturing through a variety of means
Please specify: _____
G. Promotes generic substitution
H. Promotes generic prescribing
I. Offers discounts for local manufacturers
J. Has a high price cap for generics if they are locally manufactured
K. Favours local manufacturers in tendering/procurement
Please specify: _____

L. Implements other policies supporting local or multinational manufacturers

Please provide any additional information

……
……
……

49. To what extent do you think there is awareness amongst the decision maker community regarding the international implications of ERP (for example, spillover effects in other countries, the potential for parallel trade)?

A. They are aware of these implications but are not taking them into account
B. They are aware of these implications and are seeking to minimize them
C. They are not aware of these implications
D. They are not interested in these implications
E. Other; please specify:
_____

Please expand in the space below if necessary

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……

Please also see below some more general questions regarding the region:

- Are there any countries that have different pricing rules for on-patent Vs. off-patent pharmaceuticals? If yes, which ones?

_____
_____

_____
_____

- Could you give some information regarding the Price Harmonisation policy in the GCC? Please explain the process. Is this policy mandatory and how does it relate to the ERP used in the different countries?

_____
_____
_____
_____

- What is the impact of the Price Harmonization policy in the GCC on issues such as affordability, access to medicines, price levels, etc? Any other issue? Are there any international implications from this policy?

_____
_____
_____
_____
_____

- In Qatar and Kuwait, is the country of origin still used as a reference? If not, what countries inform the reference basket?

_____
_____
_____
_____
_____

Appendix 3: Stakeholder Interview List

Country	Organisation	Stakeholder title	Sector
Egypt	Sandoz	Regulatory Affairs Executive Associate	Multinational company
	EVA pharmaceuticals	Regulatory Affairs Manager	Local company
	Pharmaceutical Manufacturing Chamber and CEO of Eva-pharma	Deputy Board of Directors	Manufacturing association and local company
	CAPA (2015-17)	Former Associate Minister for pharmaceutical affairs and Previous Member of the pricing committee (2015-17)	Regulatory body
	Ministry of Health	Head of Pharmacoeconomic Unit, Central Administration for Pharmaceuticals	Regulator
	Janssen	HEMAR Manager	Multinational company
Jordan	Joint Procurement Department of Pharmaceuticals and Medical Supplies	Director General	Regulator
	Drug Stores Owners Association	Secretary General	Product Supply Institution
	Jordanian Association of Pharmaceutical Manufactures (JAMP)	Secretary General	Manufacturer Association
	Health Coalition for Patient Protection	Secretary General	Patient Association
	Jordan Food and Drug Administration	Director of Pharmaceuticals	Regulator
Morocco	MAPHAR pharmaceutical Laboratory	Director of General Affairs	Manufacturer
	Moroccan Association of Generic Médications (AMMG)/ Polymedic Laboratory	President	Manufacturer
	Directory of drugs and pharmacy – Ministry of Health	Chief of Division of Pharmacy	Regulator
	Moroccan Association of pharmaceutical Industry (AMIP)	Director	Manufacturer Association

	Department of Planning and studies, Ministry of health	General Director	Regulator
	Department of Pharmacy and Drugs, Ministry of Health	General Director	Regulator
	Department of Tunisian' Society of Pharmaceutical Industries (SIPHAT)	Pharmacist and Head of Research and Development	Regulator
	Division of Trade, Management and supply, Tunisia Central Pharmacy	Chief Executive Officer	Regulator
	Janssen	Head of Market Access & Public Affairs Morocco, Tunisia & French speaking Africa	Multinational company
Saudi Arabia	Ministry of National Guard Health Affairs	Senior expert	Regulator
	Janssen	Director, Health Economics, Market Access, Reimbursement, Pricing	Multinational company
Lebanon	American University of Beirut	Professor of Health Systems and Financing	Academic
Algeria	Institute Pasteur of Algeria	Head of Vaccines Projects & Public Private Partnerships	Academic Non-profit organisation
UAE	National Insurance Company	Pharmacy Benefit Management	Public/Regulatory
Qatar	Qatar University	Researcher	Academic
		Former Health Care Researcher	Consultant
	Ministry of Health	Department of Pharmacy and Drug Control	Regulator
Kuwait	Ministry of Health	Department of Pharmaceutical Pricing	Regulator
	Consultant	Health Practitioner	Consultant
Bahrain	Health Regulatory Authority	Specialist in Pharmaceutical Product Regulation	Regulator

Appendix 4: Healthcare and pharmaceutical financing

The financing and reimbursement policies of the countries in the MENA region are discussed in detail below, together with key elements of their respective healthcare systems. The salient features of these systems across the region are presented in the next section.

Coverage rates (in terms of proportion of population covered) vary across the MENA countries, but generally sit around 60 to 70%. The Kuwaiti system is said to have near universal coverage.

An overview of findings is provided in the table below.

	Main Authority	Main source(s) of financing			
		Government Funding	National Health Insurance programs		OOP spending
Algeria	Ministry of Health, Population, and Hospital Reform	✓	✓	CNAS CASNOS	✓
Bahrain	National Health Regulatory Authority	✓	✓	GOSI	~
Egypt	Ministry of Health and Population	✓	✓	HIO	
Jordan	Ministry of Health				✓
Kuwait	Ministry of Health	✓			
Lebanon	Ministry of Health	✓	✓	NSSF CSC	✓
Morocco	Ministry of Public Health		✓	AMO RAMED	✓
Oman	Ministry of Health				
Qatar	Supreme Council of Health (SCH)				
Saudi Arabia	Ministry of Health	✓			No copayments
UAE		✓			✓

✓ = in place; ~ = limited

Algeria

There are two national health insurance systems in Algeria: the Caisse Nationale de la Securite des Travailleurs Salariés (CNAS) for salaried employees and their dependents, which covers approximately 73% of workers, and the Caisse Nationale des Assurances Sociales des Non-Salariés (CASNOS). In 2017, government funding reached near to 650M US$ and National Health Insurance covered near to 1.8Bn US, with the remainder of spending being out-of-pocket

payments for non-reimbursed medicines and self-medication (Primary Evidence: Algeria, 2018). National health insurance covers 100% of costs for reimbursed medicines related to chronic diseases, and 80% for other reimbursed medicines. Algeria has a burgeoning private healthcare sector, though private health insurance is very limited (Oxford Business Group, 2015).

Bahrain

Bahrainis receive comprehensive healthcare free of charge, while for non-Bahrainis it is heavily subsidized (BMI, 2017j; WHO, 2007). The Bahraini healthcare system is financed mainly through revenue from the central government (WHO, 2007).

Two health insurance systems exist in Bahrain to collect and pool funds: large employers (50 or more employees) contribute (a) a fixed annual levy to the Ministry of Health, and (b) a 3% contribution of private sector employees' wage bills to the Government Organization for Social Insurance (GOSI) social insurance scheme for employee's occupational accidents and disease (WHO, 2007). Cost-sharing is limited in the Bahraini healthcare system.

Generic drugs account for a very small proportion of total drug sales (6.0%), though the share of generic drugs is reported to be slowly increasing (BMI, 2017j).

There is a small private market in Bahrain, estimated at 3 to 4% of the total healthcare market.

Egypt

The Egyptian healthcare system is highly fragmented, with many different public and private providers and financing agents. Health service management, financing and provision is delivered by the Ministry of Population and Health, and other agencies in various government sectors which operate with varying levels of independence and under different laws (WHO, 2006)[22].

The main sources of financing within the Egyptian system are general revenues and the central government budget allocated to MOHP, and direct budget transfers from MOF (WHO, 2006). However, the MOPH is still financially constrained, with structural adjustments and budgetary constraints reducing resources over recent decades. These constraints limit the Ministry's ability to achieve dominance over coverage in the health sector; of the total population, only 51% is covered by a public health service, public health insurance or social insurance, or other sickness funds (WHO, 2006, 2011, 2011a).

The Health Insurance Organization (HIO) is a government-owned entity housed under the Ministry of Health and Population, and is both a provider and financier: the HIO uses half its

[22] The main providers are government primary healthcare units and MOHP hospitals, though tertiary care is delivered predominantly THIOs and university hospitals (64). Other aspects of the healthcare system are delivered by the armed forces and Ministries of Interior and Transport.

revenues[23] to finance services it provides, and the other half to purchase services and goods from other (private and public) providers (WHO, 2006). The HIO accounts for 10% of the total health spending of Egypt (64). The HIO predominantly covers the public sector workforce, and is estimated to not reach 80% of the private sector workforce: while all formally employed workers are required to participate in the HIO, companies can opt out of the system by paying a 1% premium on worker wages (WHO, 2006). Many large companies opt out, and spending by private firms outside of the HIO scheme accounts for about 5% of total health expenditures (WHO, 2006).

Jordan

The Jordanian public health sector is composed of four main governmental parties:

- the Ministry of Health (MoH), which covers civil servants and their dependents (21% of the insured population), and administers the Civil Insurance Program;
- the Royal Medical Services (RMS), which covers military personnel and their dependents (33% of the insured population);
- the Jordan University Hospital (JUH), which covers its employees and dependents; and
- King Abdullah University Hospital (KAUH), which also covers its employees and dependents.

Other coverage is provided by the United National Relief Works Agency, which provides care for Palestinian refugees, or private insurance (estimated at around 8-10% (WHO, 2007a, 2009a). Exact coverage rates vary: the percentage of the total population receiving national or social health insurance coverage has been estimated as extending to 68% (WHO, 2009a), 70% (WHO, 2007a), or 75% (WHO, 2011b) of Jordanian citizens. The remainder of the population (between 25 to 30%) has no means of healthcare coverage. Jordan subsidizes medicines for certain vulnerable populations (pregnant women, children under-5, elderly, and people who cannot afford their prescriptions) and may provide medicines for particular conditions free of charge to the entire population.

A large proportion of the population, particularly those with no private insurance, have to pay out-of-pocket for medicines. These expenses are often within the private sector, as habitual shortages of essential medicines exist in public sector health facilities (WHO, 2007a).

[23] Revenue for HIO comes from four primary sources: (1) a proportion of employees' salaries through the Social Insurance Organization (SIO); (2) a proportion of pensioners' allowances through the Pensioners' Insurance Organization (PIO); (3) a fixed amount of school registration fees through the School Health Insurance Program (SHIP); and (4) government subsidies from general and earmarked tax revenues. HIO also receives some revenue from co-payments. (64)

Kuwait

Kuwait has universal healthcare coverage, with access to basic primary and secondary medical care covered (BMI, 2017g; WHO, 2006, 2012). This achievement of universal coverage is due to the country's small size and the resources available. The governmental public health services and medicines are provided free for citizens.

The Kuwaiti system is highly centralized, and relies almost entirely on government financing through the Kuwaiti Government and its Ministry of Finance. The country is divided into six health areas[24], each of which acts as a decentralized administrative unit with autonomy in financial and administrative affairs, health workforce training, and health delivery. Medicines and other supplies are procured centrally and then distributed to the regional facilities.

Private medical insurance can be bought in Kuwait. However, the cover provided, the exclusions and age limits of these schemes may be restrictive (WHO, 2006).

Expatriates comprising close to 50% of the total population (BMI, 2017g). Health insurance is mandatory for this group, and residence permits are not provided or renewed unless the health insurance premium is paid (or proof of private insurance is provided). Non-citizens pay a nominal user fee for healthcare services and medicines (Ball et al., 2005; WHO, 2006).

Lebanon

50 to 60% of the Lebanese population is insured either through public or private insurance (El-Jardali et al., 2017; WHO, 2012a). Box 13 presents the main financing sources in Lebanon.

Box 18: Lebanese healthcare financing

- employment-based social insurance schemes
  - the National Social Security Fund (NSSF) covers all employees of the private sector and their families. The main source of financing for the NSSF is contributions proportional to 15% of the salary (12% paid by the employer and 3% by the employee).
  - The Civil Servants Cooperative (CSC) covers regular government employees and their families. The CSC does not require any contribution from employees, bar a for 1% deduction off of the payroll.
- Security force schemes (four different schemes): funded by general tax revenues and offer full coverage for all ambulatory and hospitalization services without neither co-payment nor deductibles
- Ministry of Health financing: insures all those uninsured through other schemes
- Private insurance sector
- out-of pocket expenditures

[24] Kuwait City, Hawali, Ahmadi, Jahra, Farwania and Al Suabah

The MoH financing scheme insures all those uninsured through other schemes through taxation sources. Funded by the government budget, this scheme covers 85% of hospital bills, with full coverage payments for expensive interventions (e.g. open-heart surgeries, catastrophic illnesses drugs). The MoH financing scheme covers approximately 50% of the population (WHO, 2009b), with additional burdens being that the employment schemes cover a younger employed population and private insurance companies select healthy population groups for eligibility. This is in addition to a high burden of out-of-pocket expenditure, currently the largest source of health expenditure in Lebanon (70% of total expenditures on health (WHO, 2006b)).

Almost all public insurance schemes in Lebanon require some cost-sharing, as there is no public financing body that offers complete coverage (WHO, 2006b). The MOH fully covers drugs listed on the MOPH Formulary, provides expensive medications to patients who do not have any formal health coverage, and provides vaccines for all children free of charge (WHO, 2012a). Public funds cover all drugs on the EML for in- and outpatients. The NSSF covers 95% of costs for drugs for chronic diseases and 80% for other drugs, while the CSC provides 75% reimbursement. Other governmental bodies (e.g. military schemes) may provide 100% coverage for members. However, only around 20% of drugs consumed are thought to be reimbursed through one of the schemes, and the majority of the Lebanese population pays out-of-pocket for pharmaceutical product (WHO, 2009b).

8% of the population covered by private health insurance (WHO, 2012a), and there are 70 insurance companies that provide health insurance (WHO, 2006b). In private insurance, patients paid the full cost of pharmaceuticals, though these expenses have decreased from 60% in 1998 to 37.34% in 2012 (Primary Evidence: Lebanon, 2018). The private sector is not required to provide coverage for the EML.

Morocco

Since 2002, Morocco's healthcare system has had two health insurance mechanisms:

- compulsory health insurance system (AMO)
- the Medical Assistance Plan (RAMED): covers the medical care of the poorest sections of society. (Brahmi et al., 2016)

Medicines represent about 47% of public health insurance expenditure (BMI, 2016d). Public sector hospitals reimburse generics at 100%, while CNOP reimburses pharmaceuticals around 70-100% and CNSS covers around 70-90% (Kanavos et al., 2018). The private sector reimburses at around 90%.

Household OOP payments are made mainly for the purchase of drugs and other medical products for self-medication, prices and prescription customs, and is exacerbated by low health insurance coverage (WHO, 2006c).

Private insurance companies cover the employees of a few private firms through group health insurance contracted by the companies. Premiums vary based on the coverage selected and are determined as a percentage of the salary bill using fixed rates.

Oman

The Ministry of Health is the principal provider of preventative, promotive and rehabilitative services, providing up to 80% of the health care in the country (WHO, 2004). Care provided through government institutions is free for Omanis and for expatriates working in government services. The Ministry of Health's services are almost universally accessible: almost all health care components have reached nearly 100% coverage (WHO, 2004). At the point of delivery, are may be co-payments for consultations, but not for medicines (WHO, 2011d).

Drug control, bulk procurement and distribution of drugs are managed by MoH (WHO, 2004).

Private insurance schemes provide medicines coverage, but are not required to provide (partial) coverage for medicines that are on the EML (Alrasheedy et al., 2013; WHO, 2004).

Qatar

Seha, a national health insurance policy, was launched in July 2013. Under Seha, the government was responsible for insuring nationals, while companies were responsible for insuring expatriates they employ. All health insurance premiums for Qatari nationals were paid for by the government of Qatar, while private insurers provided supplementary health benefits (BMI, 2017i).

Since healthcare costs continued to increase rapidly, the Seha model (of almost free medical services) became unsustainable. Seha was suspended in December 2015, and was expected to be replaced in 2017. As of December 2017, no additional information on the new health insurance scheme had been released. Qatar's healthcare system will become increasingly privatised following the suspension of Seha (BMI, 2017i).

The Hamad Medical Corporation (HMC) is the primary provider for health care in Qatar. The government covers all costs for Qatari nationals, and provides partial coverage for non-Qataris. All residents in Qatar with a Hamad medical card are dispensed free pharmaceuticals (for Qataris) or required to pay a 20% copay (non-Qataris). Residents and visitors without the Hamad card pay 120% of the value of dispensed pharmaceuticals. Most patients receive medications from one of the eight hospitals run by HMC after a nominal charge of QR 2.0-10.0. (Awaisu et

al., 2014). Private health insurance covers services at private hospitals, and medicines are fully covered (Awaisu et al., 2014).

Saudi Arabia

In Saudi Arabia, health care services are provided primarily by the Ministry of Health, though the Ministry of Defense and Aviation, the Ministry of the Interior, the Saudi Arabian National Guard, the Saudi Arabian Oil Company, and other governmental agencies, also finance and deliver primary, secondary, and tertiary care (Al-Aqeel, 2012; Bawazir et al., 2012; Khan et al., 2016).

Under Saudi law, Saudi citizens are entitled to free healthcare, and services offered by public hospitals are free of charge for all eligible citizens (Al-Aqeel, 2012; Bawazir et al., 2012). Free medical coverage is also provided to all citizens and expatriates working in the public sector (Al Hussein et al., 2009; Bawazir et al., 2012). All citizens can receive medicines free of charge in governmental healthcare facilities, and the public healthcare system or social health insurance schemes provide medicines free of charge for certain conditions (BMI, 2016e). They do not pay any fees or co-payments for medicines. 69% is covered by a public health service, public health insurance or social insurance, or other sickness fund (Alkhuzaee et al., 2016; WHO, 2012b).

Health care financing in Saudi Arabia is provided mainly from government revenues, with other sources being private sources (e.g. out-of-pocket payments) and from occupational health insurance premiums provided by large private company employees (WHO, 2006d).

There is a large private sector in Saudi Arabia, which operates independently at all levels and sets its own fees for the services they provide (Khan et al., 2016). 31% of the population is covered by a private health insurance. Private health insurance schemes are required to provide at least partial coverage for medicines that are on the Saudi National Formulary (WHO, 2012b).

UAE

Currently the UAE has a comprehensive, government-funded health service administered by the Federal Ministry of Health, accompanied by a developing private health sector (WHO, 2006e). The funds provided by federal health institutions are supplemented by contributions from local governments, especially the local Government of the Abu Dhabi Emirate. Additional funding is sourced from earmarked funds for capital expenditures, the Armed Forces, the resources of the Emirate of Dubai, and private expenditure.

Other agencies provide resources to spend on their own medical services, including the health services of the Military by the Ministry of Defense budget and oil companies with their own medical services for their staff and dependents.

Medical care in government health facilities was free of cost to patients until 1993, when health cards were introduced: patients are required to possess a health card in order to access the government health care system (at a fee of AED 100 (USD$ 27) per year). For expatriates (non-UAE nationals, which currently comprise 80% of the population), a payment of AED 300 (USD$ 82) per year provides a health card[25] to access to medical services MOH facilities for minimal copayment fees for services and medicines.

[25] The health card is a mandatory requirement for expatriates to receive a work permit in the UAE

Appendix 5: World Bank Income Classification

Country	Classification
Algeria	Upper middle income
Bahrain	High income
Egypt	Lower middle income
Jordan	Upper middle income
Kuwait	High income
Lebanon	Upper middle income
Morocco	Lower middle income
Oman	High income
Qatar	High income
Saudi Arabia	High income
UAE	High income

***Source**:* World Bank, 2018.

Thresholds for country classification by income, as of 1 July 2017:

Threshold	Gross National Income/Capita (current US$)
Low income	< 1.005
Lower middle income	1,006 – 3,955
Upper middle income	3,956 – 12,235
High income	> 12,235

Source: World Bank, 2018.

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