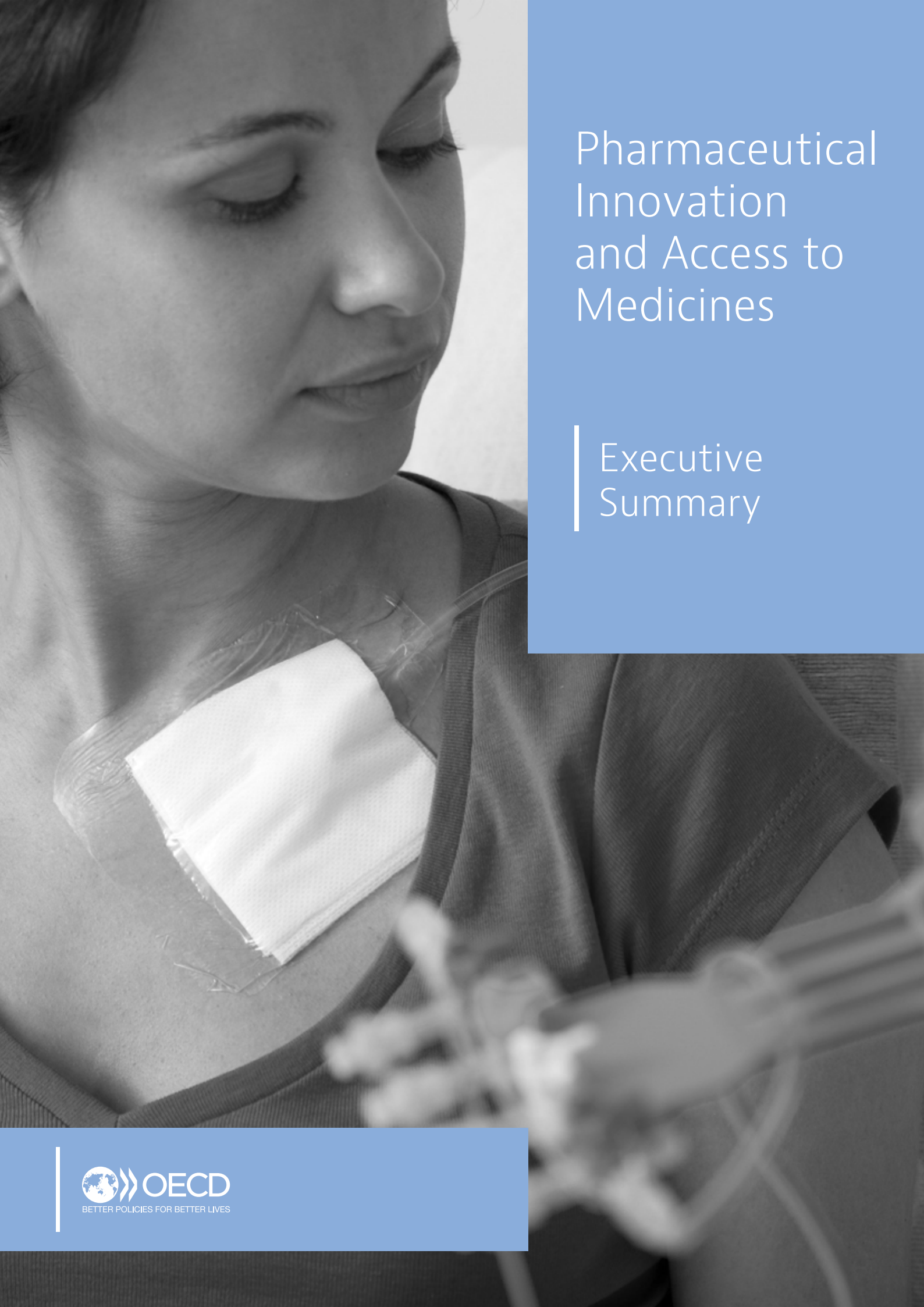


Pharmaceutical Innovation and Access to Medicines

Executive Summary

OECD
BETTER POLICIES FOR BETTER LIVES

Contents

This document is an Executive Summary…

…of the OECD report on Pharmaceutical Innovation and Access to Medicines. It provides an overview of the key insights of the report, which draws on an evidence-based assessment of the current performance of the pharmaceutical innovation system, and presents a critical analysis of policy options for reforms to promote access and sustainability.

Introduction

In recent decades, novel medicines have not only improved survival rates and quality of life for many patients around the world, they have also changed the natural history of diseases such as HIV and certain cancers. Anti-retroviral therapies have transformed HIV from a terminal illness to a manageable chronic disease, while the once-daily single tablet regimen has simplified the daily lives of patients. In the last 15 years, the 5-year survival rate for patients with chronic myeloid leukaemia has improved from less than 20% to more than 90%, thanks to the advent of a class of drugs known as tyrosine kinase inhibitors (TKIs). With direct acting anti-virals (DAAs), hepatitis C, once the leading indication for liver transplant, is now curable in more than 90% of treated patients with as little as 8-12 weeks of treatment.

> Sustainable access to innovative medicines is a source of growing concern.

Despite these undeniable advances, both policy makers and other stakeholders in many countries have become increasingly concerned about the outputs of the pharmaceutical innovation system. The prices of many novel drugs make affordable access to them very difficult for both payers and patients; the R&D process is costly and complex; the expected market rewards are sometimes insufficient to incentivise the development of some badly-needed products; the costs and pricing structure of the pharmaceutical market are often opaque; and there are legitimate questions about the degree of innovation and value offered by certain increasingly costly new treatments. Over time, these issues have affected the trust some payers and other stakeholders have in the pharmaceutical sector, and at the same time have prompted concern as to whether existing policies can promote the development of major innovations while ensuring sustainable access. Increasingly, there are calls to reform the system.

In 2017 the OECD received a request from Health Ministers of its then 35 member countries to prepare a report that highlights the main challenges governments and other stakeholders are facing in ensuring appropriate access to novel medicines to all those in need, at a reasonable cost, while maintaining incentives to innovate. The purpose of the OECD report is to provide evidence of how well the current system is performing, based on objective measures and evidence-based analyses, and to assess critically policy options for reforming the system.

While this report focuses on medicines, it is important to place its assessment in the broader context of enhancing value for money in the health system as a whole. Indeed most, if not all OECD countries are facing significant challenges to keep health spending under control. Containing health spending, while enhancing access to, and quality of, health services, requires bold action to reduce the waste that permeates health systems. A recent OECD report on "Tackling Wasteful Spending on Health" (OECD, 2017) highlighted that a significant proportion of health spending in OECD countries is at best ineffective, and at worst, wasteful. It suggested ways to address waste in many areas, notably by improving appropriateness of care, and tackling duplication and inefficient processes. At the same time, the pharmaceutical sector can play an important role in this general effort to improve value for patients, while exploiting all the potential offered by new technologies.

How is the current system performing?

The pharmaceutical industry plays an important role in a number of OECD economies, directly employing more than 1.2 million people, of whom nearly half a million are in the United States. The industry also represents a significant share (0.8-0.9%) of total employment in countries such as Switzerland, Slovenia and Denmark. Among the sectors with the highest R&D-intensity, the industry invests up to around 40% of its gross value added (GVA) in R&D in Japan and the United States. Pharmaceutical industry R&D accounts for 30% of all private R&D in Switzerland and Belgium, and 24-25% in Slovenia and Denmark. Globally, more than three-quarters of all clinical trials of medicines and other health interventions take place in OECD countries.

> Policy makers are trying to find a balance between promoting and rewarding innovation, ensuring access to medicines, and sustaining the viability of health systems.

Pharmaceutical R&D is risk-prone, costly and time-consuming, and although the contribution of the public sector is significant, much of the risk and costs are borne by private enterprises and investors. Successful development of a new medicine takes an average of 10 to 15 years. The probability of obtaining marketing approval for a drug entering phase I clinical trials ranges from 7% to 45%, depending on the type of drug and approval process. The productivity of pharmaceutical R&D, measured as the amount spent per approved medicine, has declined – as it has in other research-intensive industries, partly because "ideas are harder to find". Only a minority of drugs that gain approval achieve commercial success. Of 466 novel active substances launched in the United States between 1991 and 2009, half achieved life-time sales of less than USD 1.5 billion, and only approximately 10% had sales exceeding USD 10 billion.

Retail pharmaceutical spending accounted for 1.4% of GDP across OECD countries in 2016 and for 2% or more in four countries (Greece, Hungary, the United States and Japan). This share has, on average, remained stable over the past decade, while the share in current health spending has decreased from 19.2% in 2006 to 16.5% in 2016. Total pharmaceutical spending is actually 9 to 30% higher than that, taking into account drugs dispensed in hospitals or administered in physician settings. In real terms and on average in OECD countries, retail pharmaceutical spending growth has been declining almost every year from a high of 8% growth in 2001 to negative growth rates after 2009 - due in part to the impact of large numbers of patent expiries and the effects of cost-containment policies - before a rebound to growth in 2014. Over this period, real expenditures in other parts of the health system, such as outpatient and inpatient care, continued to grow.

Pharmaceutical spending can represent good value for money in health systems. Beyond the therapeutic value of new products, many relatively inexpensive medicines delay or prevent disease complications and reduce the use of costlier health services. Non-adherence to treatment has been estimated to cost EUR 125 billion in European countries and USD 105 billion in the United States.

However, sustainable access to innovative medicines is a source of growing concern. The high prices of many new medicines are hitting media headlines, as they did some 30 years ago when new HIV treatments were introduced, and a decade ago with breast cancer therapies. Today, concerns about prices and affordability have been driven by a series of events that have shaken the confidence of both payers and patients, and imposed additional stresses on policy makers trying to find a balance between promoting and rewarding innovation, ensuring access to medicines, and sustaining the viability of health systems.

Four main challenges have been identified:

Despite a slowdown in growth in the 2000s, pharmaceutical spending has nevertheless increased sharply in some therapeutic areas, such as oncology and certain rare diseases where many new medicines target small population groups and command high prices. While these may well address unmet needs, they often have prices that may not be justified by the health benefits they confer.

Countries may be ill-prepared for the arrival of novel medicines targeting wide population groups. In 2013, the first of a new class of very effective but expensive drugs known as direct-acting anti-virals (DAAs) for hepatitis C created a shock due to the potential budget

impact of treating all infected people. Many countries initially restricted access to the most severely affected patients, creating frustration among patients and clinicians alike. Although subsequent entries of alternative products have created competition on prices and allowed payers to expand eligibility to treatment, the initial shock highlighted the lack of readiness of payers for such events.

In some countries, sudden, large price increases for off-patent medicines have made important treatments unaffordable for patients.

Finally, innovation is lacking in certain areas of high-unmet need, such as new antimicrobials, non-vascular dementia, and some rare diseases.

Discussions around some of these issues have been difficult in many countries, and have exposed a fifth challenge: that trust between payers, civil society and pharmaceutical companies has been eroded. Rebuilding confidence among all stakeholders on how the pharmaceutical market works is necessary if they are all to work together to ensure that the system delivers the right innovations, to the right patients, at the right prices in the future.

What could be done to make the system work better for all?

In determining how to address these challenges, this report is guided by five broad principles:

1. **Increasing the value of spending on medicines.** The overall objective is to ensure that maximum value is obtained from the expenditure made. This could lead to reduced (or curtailed) expenditure on low value items and/or increased expenditure on high value items; it may mean seeking to reduce prices (to ensure a desired level of cost effectiveness) or varying payment methods; or it may involve varying the ways in which certain products are deployed within the health care system. While payers may wish to reward innovation explicitly in order to encourage further, effective private investment in research and development (R&D), at the same time they may wish to send clear signals intended to guide investment toward the kinds of innovations that reflect *their* priorities.

2. Ensuring access in countries at different levels of development. The most effective way of ensuring that patients in countries at different levels of development can access innovative treatments is to apply differential (or tiered) pricing. Under this paradigm, more affluent countries pay higher prices than poorer countries and firms are able to earn sufficient profits in affluent countries to make further investments in R&D.

3. Supporting a rules based system. The development and application by public payers of transparent criteria for determining willingness to pay for added health benefits could enable developers to know in advance what level of reward they might expect.

4. Fostering competition in both on-patent and off-patent markets. More competition would improve the efficiency of pharmaceutical spending and provide incentives to innovate. On-patent competition is not always possible, even where there are multiple therapies for the same indication, but could be facilitated with appropriate procurement and payment policies.

5. Promoting better communication and dialogue between payers, policy makers, pharmaceutical companies, and the general public would increase trust among stakeholders and improve alignment of industry R&D with societal priorities. Policy debates and decisions need to be informed by authoritative information on industry activities, R&D costs and forthcoming products.

This report assesses a number of policy options against these principles. Given the complexity of the pharmaceutical system, there can be no quick fixes, and most – if not all – options offer advantages and disadvantages. It is a matter for countries – individually and in some cases collectively – to decide how these should be balanced. This report does not advocate or recommend any of these policy options; rather, its purpose is to inform a policy debate and facilitate the aggregation of policies into packages that improve the system, so that valued innovations can be developed that are both accessible and affordable. The policy options are described under five broad headings (A-E). The underlying analysis supporting these options is presented in the remainder of this report.

Policy options

A. Involve stakeholders in joint efforts to reduce the costs of R&D and accelerate market access

While companies are continuously seeking efficiency gains in their R&D processes, regulators could work on harmonising approval requirements, accelerating and streamlining evaluation processes, supporting information and work sharing, and in some cases, engaging in mutual recognition across national agencies. Such efforts have the potential to reduce the costs of R&D, promote both faster access for patients and earlier returns for manufacturers. However, to enhance financial sustainability for payers, any such measures would need to be accompanied by reduced prices and concomitant improvements in the value proposition.

Harmonising regulatory requirements, and encouraging mutual recognition. This measure has the potential to reduce the number and costs of clinical trials. The challenge lies in gaining agreement among agencies on appropriate methods and outcome measures.

Accelerating market access for medicines with significant potential benefit. The US Food & Drug Administration (FDA) and the European Medicines Agency (EMA) have already implemented various approval pathways to accelerate access to market for treatments for unmet medical needs. These processes work quite well, though some experts have expressed concerns about manufacturers' compliance with requirements for the submission of post-marketing studies of medicines approved through these routes. Ensuring compliance and availability of appropriate patient information are essential for this to work for the benefit of patients, payers and industry.

B. Increase spending efficiency

Increase spending efficiency in all parts of health systems, including the value and efficiency of spending on both novel and existing medicines. In the pharmaceutical sector, policy makers could consider:

Facilitating cooperation in health technology assessment (HTA). Many countries use HTA to inform coverage and pricing decisions. HTA is a complex undertaking, requiring appropriate resources and skills. OECD countries have very different capacities in HTA and duplication of effort is widespread. There is thus a rationale for promoting international co-operation in HTA activities, though arguably this may only be feasible at regional level and among countries with similar standards and patterns of care. It also requires agreement among HTA agencies on methods and approaches to be used. Collaboration and cooperation in HTA can potentially reduce administrative costs for agencies and compliance costs for manufacturers, and accelerate access to treatment. However, economic aspects of HTA will always need to be evaluated at national level, informed by local data on burden of disease, resource utilisation, and patterns and costs of care.

Encouraging cooperation in price negotiations, contracting or procurement. Already occurring to some extent (for example, the BeNeLuxA agreement in Europe, the South America/PAHO arrangements), this could increase the bargaining power of buyers, enhance competition among sellers, and impose greater discipline in negotiation and pricing processes through improving the information available to buyers. The idea is to reduce transactions costs in determining prices and/or assessing benefits, thereby benefiting participant countries (by increasing their negotiating power) and manufacturers (by reducing transactions costs). However, countries may need to be of similar income level and/or willingness to pay in order to protect the principle of tiered pricing, or additional agreements will be needed as to how prices should vary across countries.

Assess the performance of medicines in routine clinical practice and adjust coverage conditions and prices. Health system capacity to assess the performance of new technologies in routine practice is increasing. Routinely collected data could be harnessed to evaluate the effectiveness of medicines outside the clinical trial context, and to assess comparative performance. These assessments could

inform not only clinical practice guidelines, but also coverage and pricing. This would increase efficiency and value in pharmaceutical spending. The main constraint is methods development; observational studies do not always provide the information needed to assess the impact of a single product.

Promoting competition in on-patent markets. Competing health insurers or pharmacy benefit managers typically use formulary management to foster competition in on-patent markets. Price concessions from pharmaceutical companies are negotiated in exchange for "preferred status" on their formularies; this is associated with lower patient contributions and thereby encourages use of these medicines. Monopsonist purchasers often do not exploit competition in on-patent markets. Tendering is widely used in off-patent markets or/and for hospital purchases, but is uncommon among patented products. One exception is Norway, which is now tendering by indication in on-patent markets (e.g. medicines for treating hepatitis C). While tender outcomes allow for multiple suppliers – to ensure physicians and patients retain some therapeutic choice and to maintain multiple suppliers in the market – company bids determine which medicine is recommended as the first-line treatment.

Exploring bundled payments for episodes of care, for example in oncology. Such payments offer a single payment, based on the expected costs of a bundle of services used for a clinically-defined episode of care. They are expected to incentivise providers to use the most cost-effective treatment for a given pathology and to negotiate procurement prices with companies. Payments per episode of care are being piloted in oncology in the United States. While thus far these have shown encouraging results in terms of both efficiency and quality of cancer care overall, they do not necessarily give rise to savings in drug costs.

Promoting competition in off-patent markets. Competitive off-patent markets can deliver savings without loss of benefit for patients, by moving prices closer to marginal costs of production and increasing penetration of generics and biosimilars through incentives for prescribers, pharmacists and patients. A number of policies can promote uptake of generics and biosimilars, such as encouraging early entry of new suppliers upon loss of exclusivity (LoE) of originator medicines, streamlining marketing approval, encouraging physician prescribing by international non-proprietary name (INN), strengthening the role of pharmacists, and incentivising and educating patients. In addition, price competition can be fostered by appropriate procurement mechanisms, provided several manufacturers are active in each market segment. Mechanisms to influence the prices of generics could use competitive processes, such as tendering, that aim to balance short- and long-term savings, sustain competition and prevent manufacturers from gaining market dominance, which could lead to higher prices or shortages in the longer run. Sole-supplier arrangements should be avoided, as they can lead to market exit of suppliers, risking security of supply and creating monopolies that might increase prices in the long run. Finally, countries could also implement a system to monitor market dynamics and allow purchasers to report sharp price increases when they occur.

C. Determine willingness to pay for new treatments and health benefits

Governments and public payers could benefit from determining how much they are willing to pay for new treatments or for health benefits. Transparent and procedurally fair processes for defining willingness to pay might help to ensure that coverage and pricing decisions are understood and accepted by all parties. They could also increase the returns from current spending, better align spending with public priorities, improve the bargaining power of national authorities and payers, and provide greater predictability of decisions to the industry. Policy makers could consider:

Defining explicit criteria for coverage and pricing. Willingness to pay for a given drug may legitimately vary across countries and across therapeutic areas (e.g. higher willingness to pay for severe or rare diseases). Criteria considered could include not only cost-effectiveness (to reflect value), but also budget impact and equity considerations. When determining a 'value based willingness to pay', countries might also need to consider how the benefits of a new medicine compare with the benefits obtained from the same amount of additional spending on other health interventions or services – particularly when those healthcare services are being funded from the same revenue source. Value-based pricing is appealing in that it enables industry to be rewarded for the most effective medicines and ensures that the development of medicines with low value is not over-compensated. A rules-based process to making coverage and pricing decisions could also provide for resolution mechanisms when negotiations fail to reach agreement (e.g. as in Germany).

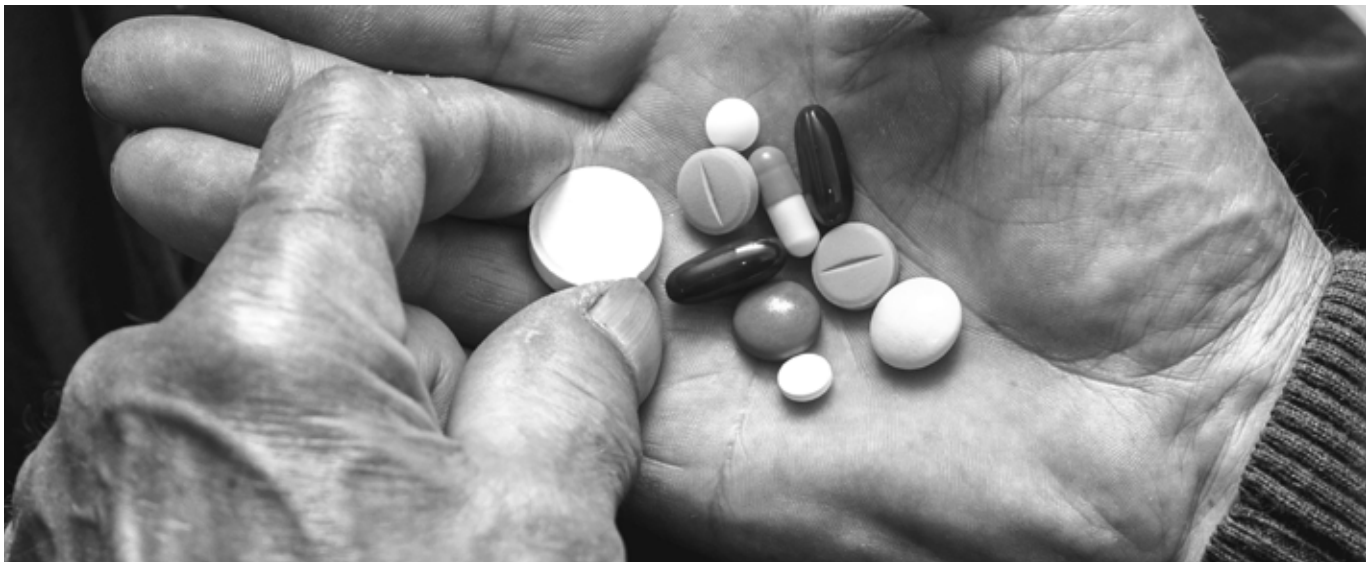
Special rules when the budget impact is high. The general principle of pharmaceutical pricing should be to reward good value. But occasionally – as with sofosbuvir (Sovaldi®), a medication used for the treatment of hepatitis C – the combination of extremely high therapeutic value and significant burden of disease led to a potentially explosive budget impact for payers, with negative effects on access. The set of criteria referred to in the previous point could include particular rules, defined in advance, on how to behave in such (albeit generally rare) situations. For example, payers could propose a capped budget and negotiate with the company to supply, within that expenditure cap, all those needing treatment (as was the case in Australia with hepatitis C treatments, for example). They could also propose that payments be phased over several years, in order to accommodate budget cycle constraints. Such policies do not undermine the need to reward innovation appropriately, since the total returns in such cases may still be very high. However, by determining the magnitude and phasing of large expenditures in advance, greater certainty is provided to both manufacturers and payers. Governments and other payers could, for example, begin to consider how they would manage the advent of one or more effective treatments for a highly prevalent condition such as Alzheimer's disease.

Optimising the use of Managed Entry Agreements. Performance-based managed entry agreements are used in many countries but their implementation has not always been ideal, with difficulties in outcome measurement and high administrative overheads. Such agreements could be better utilised, by being limited to products whose effectiveness or cost-effectiveness is highly uncertain at the time of launch, and where the additional evidence can shed light on their value. Outcomes could be better defined and measured, and results shared with the scientific community, prescribers and patients. Ideally, agreements should be designed to incentivise firms to demonstrate the performance of their products. This could, for example, involve setting initially low default prices or partial payments, with price increases or additional payments made if and when evidence demonstrates that pre-defined performance targets have been met. Such agreements have the potential to increase the knowledge base for medical products, and to ensure payers pay for value. They should not, however, supplant randomised control trials as the primary source of evidence from which to assess efficacy, effectiveness, and cost effectiveness.

D. Develop new push and pull incentives for innovation

New push and pull incentives could be developed to encourage innovation in areas of high unmet need, such as antimicrobials, non-vascular dementia and rare diseases. Options include:

Developing push incentives targeting product development addressing unmet medical needs and attaching access conditions to public funding of R&D. The public sector already contributes to R&D funding through various mechanisms (R&D tax credits, direct funding of basic research or of clinical trials, Public-Private Partnerships and Product Development Partnerships). It could prioritise investment in research that is unattractive to the private sector. Where the public sector contributes



substantially to the development of specific products, affordable access could be assured through voluntary licencing or patent buy-outs.

Exploring alternative pull incentives to encourage R&D addressing unmet medical need. This is particularly necessary to tackle antimicrobial resistance and rare diseases. The existing system of rewards based on volume of sales cannot work for new antimicrobials, and countries need to explore other mechanisms such as market entry rewards, prizes and advance market commitments.

Reviewing orphan drug policies to target more closely areas of unmet medical need. The number of medicines and indications available to treat rare diseases has been increasing over time. While this is good for patients with rare diseases, orphan designation (with associated advantages) is sometimes granted for products with multiple other indications that generate 'blockbuster' revenues. The development of precision medicine implies that indications will target increasingly small populations, making them potentially eligible to receive advantages arising from orphan drug policies. These advantages often come at a cost to taxpayers, through reduced or absent evaluation fees, tax credits, and extended market exclusivity in some countries. Current trends suggest that these costs will increase, without necessarily spurring development of the types of medicines for which these advantages were originally intended. It may be useful to assess whether existing orphan drug policies are delivering the right incentives and outcomes, and to assess alternative options.

E. Strengthen the information base to better inform policy debates.

Despite the complexity of assessing with precision the costs incurred in successful and unsuccessful product development, both payers and the general public need a better understanding of the costs involved in developing new medicines, how these costs are incurred, and the magnitude of the returns investors and companies earn from these activities. Payers also need intelligence about company pipelines to prepare for the impact of forthcoming treatments on both systems and costs, particularly transformative treatments with high costs and budget impact. Progress in this domain requires action on a broad front, including:

Publishing authoritative information on industry activities and the risks, costs and returns from R&D, to better inform policy decisions. Policy debates are often confounded by contradictory data and polarised views on the role and performance of the industry. Divergent views are legitimate, but the publication of relevant and authoritative information could inform a more constructive debate. The OECD could mobilise its wide expertise (including in health, innovation and technology and finance) and its privileged relations with governments and industry to develop consensus on relevant indicators and data collection (e.g. primary data collection as well as the use of existing databases).

Increasing price transparency in pharmaceutical markets. Levels of price opacity in pharmaceutical markets are high and increasing, both within and between countries, in part due to the proliferation of confidential agreements between the industry and private and public payers. The disconnect between list prices and transaction prices has a number of drawbacks: high list prices serve as an anchor in all price negotiations; they blur international benchmarking, which is used by many countries; analyses of price trends become uninformative, and manufacturers may be criticised for high list prices that do not apply in reality. Full transparency might be difficult to reconcile with tiered pricing, because the pressure from public opinion in countries with high ability and willingness to pay to reduce prices to match those obtained elsewhere, may be intense. To balance these concerns, a first step would be for purchasers to indicate publicly the existence of pricing agreements on specific products. Ex-post and transparent rebates for public payers are another option, which would be compatible with both value-based and tiered pricing.

Improving horizon scanning activities and encouraging co-operation at regional level. A number of countries have recently engaged in horizon scanning activities to better prepare for market launches and adoption of new technologies, sometimes involving regional co-operation. International co-operation in horizon scanning could help improve methods and sharing of information on the R&D pipeline and forthcoming treatments, as well as information on dates of patent expiries and loss of market exclusivity. Companies would benefit from countries being better prepared for the diffusion of new treatments.

Contact, References, Acknowledgements

For further information

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Pharmaceutical Innovation and Access to Medicines

The OECD report on Pharmaceutical Innovation and Access to Medicines reviews the important role of medicines in health systems, describes recent trends in pharmaceutical expenditure and financing, and summarises the approaches used by OECD countries to determine coverage and pricing.

It then highlights current issues for policy makers, such as the increasing prices of new medicines; concerns about the value of spending in some therapeutic areas; challenges in anticipating the arrival of very effective medicines for highly prevalent diseases; sharp price increases in off-patent products; and the apparent misalignment of current incentives for the development of treatments for certain conditions.

The report also describes the role of the biopharmaceutical industry in OECD economies, examines the process of pharmaceutical R&D and its financing, and looks at the risks, costs and return from R&D investment for the industry. Examining trends in the industry over time, it shows that productivity of R&D expenditure has declined; that the duration of market exclusivity has remained relatively stable; that new medicines are increasingly being developed for small patient populations; and that the industry as a whole has remained highly profitable for investors.

Lastly, the report presents a range of policy options for consideration by policy makers, to support the development of effective and co-ordinated responses to the identified challenges.

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