

Equitable Pricing of Medicines
Students for Global Health National Policy (2020)

Note: *This policy complements the submitted policy entitled 'research and development for access to medicines'.*

Introduction

Access to affordable medicines, which includes pharmaceuticals, vaccines and diagnostics, is essential to achieving Universal Health Coverage, as well as developing sustainable and equitable health systems. Despite this, the price of medicines is rising globally and becoming an increasingly concerning issue. Unfair and inequitable pricing hinders access to medicines and public health across the world. More broadly, a monopoly based model of financing global pharmaceutical R&D has resulted in high prices and research gaps.

SfGH position

SfGH recognises the fact that equitable pricing represents a reasonable and sustainable price for both buyers and sellers, which maintains affordable access to medical products whilst also stimulating innovation and research. However, in the current climate, it should be noted that the pharmaceutical pricing system heavily favours the sellers, denying the buyers access, affordability and power over medicines that are essential for health and wellbeing of individuals and populations. Thus, SfGH believes that the focus of equitable pricing discussions should be not only on reducing the monopolistic power of the pharmaceutical industry to facilitate equitable pricing within the current pharmaceutical system, but also on exploring new models of financing research and drug development in ways that do not rely on high prices, so that innovation and access can co-exist successfully.

Calls to action

Students for Global Health UK therefore calls on:

The UK government to

- Continue to ensure the financing of medicines in the healthcare system in an equitable fashion
- Monitor, collect, and publish data on the affordability, availability and quality of drugs purchased for the NHS
- Explore new models for the tendering and procurement of medicines which reduce costs and improve buyer negotiating power
- Use their significant negotiating power to drive down drug prices to an affordable and sustainable level, and make these prices publicly available
- Protect and promote the introduction and substitution of generics and biosimilars to prevent monopoly and increase competition, for example by streamlining regulation and approval
- Protect and strengthen the government's existing rights to control drug pricing and cost-effectiveness analysis for drugs used in the NHS, including in any future free trade agreements

- In order to ensure access to originator medicines, use TRIPS flexibilities such as compulsory licensing or Crown-use licensing, where a cost-effective price cannot be agreed upon with, within a reasonable period,
- Refrain from using political pressure to deter other countries from using TRIPS flexibilities so and reject the inclusion of TRIPS-plus provisions in future free trade agreements
- Protect and strengthen the current Health Technology Assessment mechanism in the UK, NICE, to ensure affordable medicine prices for the National Health Service and other healthcare providers, and make the process of cost-effectiveness evaluation transparent
- Implement and enforce legislation to improve transparency in the costs of research and development. For example, by mandating the publishing of the costs of research, development and manufacture of medicines.
- Implement and enforce legislation to improve the publishing of clinical trial results, clinical trial registration and access to data
- Ensure that public funding of research and development of medical innovation comes with strong, legally enforceable access and affordability conditions that result in the equitable pricing of the final product
- Participate in and encourage the pooling of pharmaceutical procurement to drive down pharmaceutical prices and streamline purchasing
- Explore new and innovative forms of pharmaceutical pricing and research and development, which prioritise public health and access to medical products

Pharmaceutical industry

- Fully disclose the true costs of research and development, as well as the actual sales prices of drug
- Support and explore new models of pharmaceutical pricing and research and development which decrease the need for monopoly based incentives

UK universities

- Ensure that public funding of research and development of medical innovation comes with strong, legally enforceable access and affordability conditions that result in the equitable pricing of the final product
- Implement socially responsible licensing

National committee

- Affirm support for socially responsible licensing and equitable pricing

Local branches and SfGH members

- Lobby all relevant bodies at their respective universities to implement socially responsible licensing and to publish results of all trials carried out at their institutions
- Lobby local MPs to include equitable pricing of medicines in their manifestos
- Seek to implement socially responsible licensing and transparency in their own research

Position paper

Background

Currently, two billion people worldwide lack access to essential medicinesⁱ. This is despite the fact that equitable access to health products is a global priority and essential to achieving the sustainable development goals. “Equitable pricing” of medical products, or lack thereof, is a major factor contributing to this lack of access to medicines.

Equitable pricing is a complex and nuanced topic, which encompasses and overlaps significantly with other aspects of the pharmaceutical system, including research and development, drug shortages and healthcare systems.

The pricing of medicines is, for many treatments, increasing rapidly. Global expenditure on pharmaceuticals reached \$1.135tn in 2017, up 56% from 2007ⁱⁱ. Even adjusted for inflation, between 1981 and 2015 there were large increases in launch prices across several therapeutic areasⁱⁱⁱ. This has placed excessive pressure on health systems across the world, leaving governments struggling to purchase the medicines needed for their populations. Additionally, in many countries, especially low income countries, patients face high out-of-pocket payments. The financial burden on governments and individuals is now a problem affecting countries at all levels of income, and is set to increase with the rise of chronic non-communicable diseases. Rather than representing therapeutic improvement, this increase in prices is largely considered to be due to the monopolistic nature of the pharmaceutical system, which provides sellers with the power to set the price of a product at “what the market can bear”. For example, by 2014, the average cost of a new orally administered cancer medicine exceeded \$135,000 a year — up to six times the cost of similar drugs approved in the early 2000s, after adjusting for inflation^{iv}. This trend in cancer prices has not been accompanied by evidence of significant improvements in treatment outcomes. The increase in prices of new treatments for rare diseases is even higher - in the US in 2016, the median annual price for each patient a year treated with top selling orphan drugs was \$83 883^v.

Conversely, insufficiently profitable markets for certain conditions have led to drug shortages and a dearth of research and development into medicines which are imperative to maintaining and improving public health. This perceived lack of acceptable profit in some diseases areas has resulted in large segments of the global population being underserved by the current pharmaceutical system^{vi}. This highlights the consequences of a pricing system which is fundamentally based on high-price coupled with high-volume of sales and profit maximisation strategies, discarding public health priorities which do not meet this criteria. Rather than a failure of “equitable pricing”, this represents the flaws of a pricing system which incentivises excessive profit on the volume of sales of medicines. This high unmet medical need in research and development is discussed further in other policies.

Equitable pricing, or lack thereof, is a significant barrier to access to medicines and universal health coverage.

Defining equitable pricing

The concept of equitable pricing is a complex one, with no set definition or legal framework. Although innovation can and should lead to financial returns for those investing in research, this should never eclipse the societal benefits of a new medicine. Medicines are not ordinary goods which can be adequately priced using market mechanisms, as the price of the medicine should allow for the societal need for the product to be met. However, sellers often have the strongest price setting power when the need is greatest. Coupled with monopoly power over both new and old medicines, government intervention and regulation is often needed to prevent unequitable pricing^{vii}.

Moon et al.^{viii} propose a thorough and useful definition of fair pricing, which is separate but related to equitable pricing, based on fairness to sellers and fairness to buyers. Buyers encompass those who pay for medicines, including households, insurers, ministries of health and donors. Ultimately, the public is the buyer of medicines. The balance between fairness to sellers and buyers creates a fair pricing zone with a floor and a ceiling, within which the distribution of the surplus can favour the seller or the buyer. This equitable pricing concept is dependent on significant levels of transparency, emphasis on social good, and can be adapted to different models of research and development.

Equitable pricing also centers around affordability. Affordability can be broadly defined as the “ability to purchase a necessary product in appropriate quantities without suffering financial hardship”^{ix}. An ‘essential medicine’ is, amongst other things, a medicine that should be available “at a price the individual and community can afford”^x. Affordability in the context of the right to health and public health should not be defined by willingness to pay, but by the extent of human need for the product^{xi}. Applying affordability criteria will not create a universal price benchmark due to the widely ranging ability to pay and need of different payers.

However, there is no agreement on what financial hardship means or how it should be assessed. Financial hardship can be understood at the level of the individual or the health system / government and using a number of different indicators^{xii, xiii}.

Concepts of defining equitable pricing are extremely useful, but equitable pricing in any form is far from reality in the current pharmaceutical system, which allows excessive monopoly, secrecy and abuse of power by pharmaceutical companies, resulting in significant barriers to access to medicines which hinder progress in public health.

Part I - Why are the prices of many drugs high and rising?

The setting of drug prices nationally and globally

Mechanisms for drug pricing and evaluation vary dramatically between medicine, country and companies. Globally, however, the general trend reflects the fact that medicine prices are rarely set based on affordability, cost-effectiveness or health benefit, but on the maximum that the market can bear. Price-setting processes are incredibly opaque and very often lead to arbitrary and unaffordable prices.

Despite the wide variety of price control options available^{xiv, xv} price controls are frequently inadequate, non-existent or not implemented because of the perception that price controls

would hamper innovation and drug launches by decreasing pharmaceutical profits^{xvi, xvii}. This claim has prevented progress ensuring access to medicines.

Price setting methods at the national level include index pricing, direct price control, international reference pricing and external or internal reference pricing. To support price setting, many governments use external reference pricing, which is a price regulation tool that looks at other countries' prices to set a price in a given country. Pharmaceutical companies highly criticise this process and name it as one of the reasons for keeping effective/rebate prices confidential. Different countries have had different levels of success using these methods for national pricing policy^{xviii, xix}. In general, there is a significant lack of studies on price control mechanisms in LMICs. This may result from challenges in regulating prices in countries without strong legal systems or in countries where drug purchasing institutions do not exist.

Tiered pricing refers to the practise of setting differential prices between countries depending on their development status, although the actual prices are frequently undisclosed. Some have advocated for tiered pricing as a method to improve access and affordability in low-income countries, while sustaining innovation through higher prices in high countries^{xx}. It has been argued that increased price transparency, coupled with external reference pricing, could undermine the benefits of tiered pricing, especially for developing countries^{xxi}. However, tiered pricing has not solved affordability issues for middle-income countries in particular^{xxii}. They also maintain a monopoly based high pricing situation, instead of allowing generic competition, which frequently results in lower prices than those generated through tiered pricing.

In some European countries, Health Technology Assessment (HTA) bodies support price setting. A HTA can be considered a mechanism for setting the maximum price at which a medicine could be considered cost-effective in a given health system. In the UK and Sweden they perform cost-effectiveness analysis comparing QALYs (Quality adjusted life years) to costs, and have fixed or progressive price thresholds. Health Technology assessments are increasingly essential as countries spend more on healthcare, and the WHO recommends their use for reimbursement decision making, price setting and negotiation. However, HTAs require technical capacity and frameworks which are only available in a select number of countries^{xxiii}. Although HTA is usually seen as a separate process to medicines pricing, HTA as an input for medicines pricing and incentive for innovation is a research and policy area that requires further exploration.

For the increasing number of orphan drugs (drugs for rare diseases), regular price setting mechanisms are usually applied but fail to address the special monopolistic market conditions and often modest clinical effectiveness. Based on standard value for money criteria, prices cannot be justified, yet governments face pressure to provide the pharmaceutical to those that need it. Partly because of the ability to charge high prices, investment and approvals for orphan drugs have increased dramatically in recent years^{xxiv}.

Monopoly power as a determinant of inequitable pricing

The current profit model is based on volume of sales, which creates a system in which essential but less profitable drug categories (such as antibiotics) are underfunded and

underdeveloped, hindering effective stewardship. Pharmaceutical companies reallocate scientific talent and capacity to more profitable opportunities, thereby diminishing the expertise and economies of scale they originally possessed^{xxv}.

Increased patenting has not resulted in increased innovation for medical products, but instead many 'me-too' products are reaching the market. Drugs classified as 'me-too' drugs or as having no added therapeutic benefit are the most important driver of increased retail spending on prescription drugs and accounted for 67% of the increase associated with new drugs, and 44% of the total increase in spending on new drugs between 1995 and 2000^{xxvi}. The BMJ published a study rating barely 5% of all newly-patented drugs in Canada as 'breakthroughs'. This evidence highlights a system that rewards bringing a product to market, regardless of whether it also represents a therapeutic advance, and one which has a declining ability to effectively innovate despite dramatically increasing spending on R&D.

The patent system, which grants a time limited monopoly for the originator manufacturer of a medicine, allows manufacturers to use their market power to maximise profit, and often results in prices that are both unjustifiable and unaffordable. Time limited power was originally meant to encourage investment in research, with the time limit imposed such that other players can later enter the market and competition can drive the prices down.

Frequent, often unjustified, extensions to an already excessive monopolistic system are also common. As patents near their end, extensions, additional patents, litigations and other methods are often employed by the originator manufacturers to delay the entry of competitors into the market^{xxvii}. This practise is commonly known as patent evergreening, and results in delayed introduction of generic medicines as well as high drug prices for longer periods of time^{xxviii}. Average patent life extensions in the US have been found to be over six years^{xxix}. Other forms of monopoly extension, such as data exclusivity, also limit access to medicines.

It is not just patents, market exclusivity and data exclusivity monopolies which are increasing drug prices. Off-patent pharmaceutical prices are also increasing and rapidly in many high-income countries. This usually occurs when there is a lack of competition, but the medicine still remains essential^{xxx}.

Myths about the reasons for high prices of medicines

Most pharmaceutical companies argue that high prices are needed to recover the cost of investment into research and development. There are several issues with this argument in favour of high pricing, and yet it has frequently prevented adequate price controls and industry regulation due to a fear that reducing the profits of pharmaceutical companies will stifle innovation. Additionally, manufacturers rarely disclose their true research costs when claiming that high prices are needed to recoup said investments. In any case, rather than investing their profits back into research and development, most pharmaceutical companies invest their profits in marketing and share buy-backs, which inflate the stock price by purchasing the company's own shares^{xxxi}.

Secondly, the public sector finances a large proportion of the costs of research and development, but profits largely benefit purely the private sector. Pharmaceutical companies

fail to acknowledge the significant role of the non-profit and public sector in the financing of research and development. For example, the US National Institutes of Health have funded, in part, every new molecular entity approved in the US between 2010-2016^{xxxii}. Overall, publicly funded research accounts for 49% of global health research and 1/3 of new drugs originate from university research^{xxxiii}^{xxxiv}. As well as direct investment, governments also make sizable indirect investments, for example by tax reductions and credits, which can significantly lower manufacturer costs^{xxxv}.

Additionally, some pharmaceutical companies argue that acquisition costs represent investment in drug development, such as the cost of purchasing other firms which have developed a promising drug^{xxxvi}. This, however, is a business decision, and not a true cost of drug development.

Increasingly, the pharmaceutical industry is arguing that price is based on the value of medicine i.e. the cost to society of the disease was untreated or treated with the next-best therapy, compared to the money saved by using a particular pharmaceutical product. Prices are currently not based on the value of a medicine, with increases due to changing in pricing regulation, monopoly power and generic entry far more common determinants of a medicine's price than value. Rather than representing value added, an analysis of medicine approvals in Europe between 2000 and 2014 showed that about half of newly approved medicines did not offer additional health benefits, but were modified versions of already approved medicines^{xxxvii}.

Although research and development is a risky process, responding to this uncertainty by restricting access to medicines by enforcing market monopolies and charging high prices is neither an acceptable or suitable solution^{xxxviii}.

Lack of transparency in both pricing and research

Many have argued that improved transparency is essential to determine what the fair price of a medicine is^{xxxix},^{xl}, and that the lack of transparency around the costs and prices of medicines undermines efforts to assess the fairness of prices, and places the information asymmetry to the seller's advantage^{xli}.

Pharmaceutical companies currently do not have to disclose their research and development (R&D) costs, the cost of production, or the amount of public funding received for the development of a drug. Contrary to the arguments of the major pharmaceutical companies, who estimates are usually above one billion, Drugs for Neglected Diseases Initiative estimates the out-of-pocket expenses of producing a new medicine to be range from €4 to €60 million per treatment developed, up to and including registration.^{xlii}

Equitable pricing is hindered by an absence of reliable data on development costs, which makes it even harder to accept and negotiate with the common argument that the costs of development necessitate high prices. Transparency around development costs could shed the light on the actual cost to the manufacturer of producing a drug, as well as the substantial role of the public sector in funding research, which is often overlooked^{xliii}.

The secrecy around drug pricing globally, which masks the actual cost of products to buyers, makes it extremely difficult to negotiate effectively with sellers. Confidential discounts are common in high-income countries, and secrecy prevents all buyers from demanding the lowest price available. Additionally, middle income countries have both little market information, lack of financial support and weaker negotiating power, which significantly hampers their ability to negotiate effectively^{xliv}. Contrary to the arguments of the pharmaceutical industry, this does not necessarily allow lower prices for poorer countries, but instead favours those with the most negotiating power. Secrecy makes it hard to guard against inequity in actual prices, and may actually result in higher relative prices in low and middle income countries^{xlv}.

Greater price transparency would assist many countries in negotiating, but would also improve budget analysis, purchase choices, tendering strategies, procurement mechanisms and clearer policies on pharmaceuticals^{xlvi}. Additionally, the results of the MI four A database, which aims to increase transparency in the pricing and procurement of vaccines, has shown no obvious signs that greater transparency affects either vaccine availability or prices negatively.

Value based pricing

Value based pricing is frequently being used to justify high prices of medicines. It refers to the pricing of a medicine based on the cost to society if a disease is left untreated or is treated with second best therapy. There are several problems with this justification.

Firstly, price is not the only or necessarily the best way of assessing value. It has been questioned whether market price should be used to judge the utility of what are arguably essential public goods. Pricing in this context does not reflect a hypothetical 'supply-demand' situation, rather an unequal power dynamic in which one party has little choice but to pay the maximum price possible or suffer serious illness or death. When value based pricing is based on the assessment of willingness to pay on the part of a low-power buyer, prices are likely to inflate and exceed what is fair or affordable.

Secondly, justifying future prices based on current prices creates a positive feedback loop which rewards over-priced past medicines and results in fast-growing medicine prices.

Thirdly, where it has been practically implemented, value-based pricing has resulted in increases in price, rather than creating a price that represents public health priorities. Gilead's sofosbuvir, an exceptionally effective hepatitis C medicine, is technically cost effective based on its value, despite its famously high price^{xlvii}. It also resulted in extremely high profits for Gilead - Gilead's global sales of sofosbuvir and related combination products totalled \$59bn from 2014 through 2018^{xlviii}. In practise, value based pricing can far exceed affordability thresholds^{xlix}.

Fourthly, it is not practical to implement due to the highly uncertain and laborious process of calculating the value of a medicine and exceedingly open to abuse by manipulation of data or variables. For example, different patients have different desired outcomes and therefore a drug will have different value, and the value of a drug may be changed over time as society or the innovation space changes.

Other factors

The distribution chain for pharmaceuticals is complex and varied, and may impact the price of a medical product in a number of different ways. Although small, the contributions of supply chain costs do have a significant impact on the price of a medicine. These hidden costs include excessive mark-ups, both in the private and public sector; taxes and VAT on medicines; and tariffs and duties on the import and export of medicine. Although the manufacturer's selling price is the most important factor in determining the price and affordability of the final product, it is still recommended that VAT, taxes and tariffs are removed for medicines, especially essential medicinesⁱ.

On a health systems level, poor access to medicines is often a function of patients being forced to buy their medicines with out-of-pocket payments. Assuming a manageable cost of medicines in to a government in the first place, governments and health systems should ensure that medicines are free or minimally priced at the point of care, such that they do not create catastrophic health expenditures for patients and their families.

Part II - Moving towards equitable pricing

Reducing monopoly power and promoting competition and generic entry

One of the most important ways to reduce the price of medicinal products is to promote the introduction and use of generic or biosimilar medicines. Policies and incentives that promote competition and reduce monopolies can be very effective in improving the affordability of medicines. Competition and market dynamics are influenced by a range of policies including regulatory requirements for generics and biosimilars, enforcement of competition policies, uptake and substitutability of generics and biosimilars, and the size and saturation of the marketⁱⁱ.

To prevent the creation of unjustified monopoly power, countries should ensure that patents are only awarded for genuinely innovative products, which are new, involve an inventive step and are capable of industrial applicationⁱⁱⁱ. Additionally, policies that maintain or increase monopolies should be removed, for example patent linkage, data exclusivity, market exclusivity or allowing extensions of the patent term without genuine innovation.

A large number of pharmaceutical industry activities may fall under national and international competition law, which holds an incredibly complex relationship with IP, and multiple pharmaceutical companies have been observed to infringe competition law^{liii}. Despite this, competition law has barely been used to tackle excess or unfair prices^{liv}.

Early market entry and quick uptake of generic and biosimilar products are key to improving access to medical products. Prices of medicines with generic competition have been shown to drop up to 66% compared with the originator price, and prices of biosimilars are also much lower than their originators^{lv}. Generic medicines entering the market have notably significantly improved access to medicines for the treatment of HIV and hepatitis C in both low and middle income countries^{lvi}. Generic medicines perform better in terms of market entry and penetration in countries with mandatory generic substitution, which improves the

maximum uptake of a medicine and increases its prescription, but relies heavily on adequate trust in generic and biosimilar medicines from prescribers and patients^{lvii}. Regulatory bodies can promote access to the market for generics and biosimilars, for example by streamlining the approval process, implementing a pre-qualification process, ensuring quality and safety, and preventing monopoly extension.

Public benefits from public investment in research and development

Since a large proportion of research and development funding comes from the public sector, it is reasonable to argue that a share of the benefits should also reach the public. Mechanisms for achieving this would involve attaching conditions to public funding.

These attachments could include “reinvesting profits from innovative products to support future R&D; a commitment to share knowledge and fully disclose data related to R&D, including expenditures and data from failed clinical trials; the possibility of the public retaining a golden share from IPR (and, on occasion, equity of profits); and a requirement that manufacturers supply treatments on reasonable term”^{lviii}.

Universities also have significant ability to ensure equitable access to products that result from research conducted at their institutions, and should implement socially responsible licensing practises for all of their technology transfers.

The preferred mode of technology transfer should always be non-exclusive licensing, where as many licensees as possible are actively sought out. If this is not possible then the following strategies may be employed (as detailed in the Equitable Technology Access Framework):

- Non-exclusive licensing of the health technology, without active seeking of multiple licensees.
- Limit exclusive licenses to high-income countries and grant non-exclusive licenses in low and middle income countries
- Require that the licensee agrees to provide the health technology “at-cost” or marginal cost of production to low and middle income countries and low-income populations in high-income countries.
- Follow a non-assert policy, in which the licensee publicly declares that they will not enforce its Intellectual Property Rights (IPR) outside High-Income countries.

Improving transparency in pricing and in research and development

Increasing the transparency in the costs of research, development and production of drugs, as well as their actual prices, is essential to moving towards equitable pricing. Pooling of data and increased transparency within research and development could also reduce R and D costs and therefore has the potential to reduce price by avoiding duplication of research, improving collaboration and expanding access to innovative science.

At the World Health Assembly in 2019, a transparency resolution was passed to enhance public sharing of information on the actual prices paid by governments and other buyers for health products. It is hoped that this greater transparency will shed light on the determinants of pricing and improve negotiating power for buyers.

In the United States, where drug prices are highest, thirteen states have introduced legislation to increase transparency and some states have made it mandatory that price increases are disclosed and justified, including a disclosure of cost breakdown by R&D and marketing expenses and of prices charged in other countries. Healthcare providers have lobbied to paralyze the process, supported by medical associations and a myriad of scientific societies^{lix}.

Ideally, companies should fully disclose the public and private funding of their research and development, as well as the costs of producing a medicine, but this is unlikely to occur without intervention. Transparency can be increased and disclosure enforced through government action such as legislation, regulation, judicial action, conditions on receiving public research funds and other public investment, or listing in a formulary for reimbursement.

Promoting the use of TRIPS flexibilities

An essential part of ensuring equitable pricing of medicines and preventing excessive pricing is the use and promotion of legal mechanisms known as TRIPS flexibilities, which can be used to counteract the negative public health impacts of a monopolistic intellectual property system. It is also essential that Least Developed Countries are not required to be fully compliant with TRIPS until at least 2030^{lxxi}. TRIPS flexibilities are designed to allow some flexibility in the World Trade Organisation standards for the regulation and protection of Intellectual Property. TRIPS flexibilities provide countries with the ability to overrule or bypass some standard IP rules in order to protect public health, such as by issuing a compulsory license, which allows another party to produce a patented medicine and can result in the production of a drug without authorisation of the original patent holder^{lxxii}.

The issuance of a compulsory license, or the threat of a compulsory license, often triggers the issuance of a voluntary license^{lxxiii}. This has been used in multiple countries as an effective means of reducing the cost of medicines^{lxxiv}.

However, the free use of TRIPS flexibilities is increasingly coming under threat, both from political pressure and from Free Trade Agreements which have sought to strengthen Intellectual Property protection, although known as “TRIPS-plus” provisions^{lxxv}. “TRIPS-plus” measures such as data exclusivity, linkages between drug registration and patents, parallel import limitations and marketing exclusivity, which interfere with effective use of TRIPS flexibilities, should be discouraged and not implemented.

Pooling of procurement and patents to facilitate lower drug prices and improved access to medicines

Governments with adequately functioning health systems can use large volume procuring to pooled procurement, internationally or internationally, to pool risk and reduce prices. Pooled procurement of pharmaceuticals generally results in price reductions, better quality assurance, reduced corruption, standardisation, reduced administrative burden and access to more sustainable financing^{lxxvi}. This has been done successfully within many countries, for example using sub-national coordination and collective bargaining^{lxxvii, lxxviii}. Pooled

procurement internationally can also be effective in reducing drug prices. The Global Drugs Facility has succeeded in lowering the price of treatments for drug resistant tuberculosis by 26%, and also assists countries in what can be complex and arduous procurement processes^{lxix}.

Patent pools, in which multiple patents are licensed non-exclusively to a pooling body, were developed to improve access to medicines particularly for developing countries. The creation of such a pool results in dissemination of technology by allowing users to sign only a single license for several patents, which generally entitles paying a single licensing fee or royalty rate to the patent pool. Patent pools facilitate voluntary licensing, generic production and patent assessment support. Patent pools also lower costs, result in less license negotiation, decrease the risk of patent litigation, address the issue of blocking patents, and facilitate the development of new combinations^{lxx}. An extremely successful example of this is the Medicines Patent Pool^{lxxi}. Initiatives such as this should be strengthened and expanded, especially for middle income countries who are often excluded from these agreements.

Patent pools by themselves do not necessarily lower the price of medicines, unless the total fee that manufacturers have to pay to get the license to use all the patents in the pool is lower than the sum of the fees of signing individual licenses to use each patent. In order for patent pools to successfully fit the de-linkage model, the price of the licence to use the patent pool should:

- Not reflect the cost of research and development (this cost should be covered instead by grants and milestone prizes)
- Not reflect the will to maximise licencing revenues
- Have a licencing fee to use the patents which is affordable to non- for- profit manufacturers, or at least to enough manufacturers to create market competition

New models of pricing and research and development of medicines

Pre-market commitment has been used to attempt to solve some of the market problems, especially related to vaccines targeting developing country diseases. These pre-market commitments provide a guaranteed floor price for a fixed quantity of product as well as co-payments and top-ups to facilitate purchase by developing countries. These commitments can specify the properties of the expected vaccine and commit suppliers to long term selling prices^{lxxii}. These maintain the status quo of strong IP monopoly over medicines, as the profit is still based on volume of sales. Additionally, subscription or netflix models of pricing have also been proposed, especially in areas where a low-volume of sales is not only likely, but encouraged as part of stewardship, such as antibiotics. Selling pharmaceuticals at a cost of production + 10% profit margin has also been suggested.

De-linkage refers to the concept of delinking the cost of research and development, and other costs associated with the production of a pharmaceutical product, from the price and volume of sales of the final product. Instead of profiteering off the sales of a medicine, innovation that results in medical products that serve public health priorities could be supported by a variety of other incentives. This may include market entry rewards, prize funds grants, subsidies, open source dividends, and many other incentives.

Many of these new drug pricing models would require a significant shift from the current incentives for research and development, with the majority of profit and reward being found in areas other than the volume of sales of the drug. They therefore necessitate some element of delinkage, as well as different research incentives including push, pull and pool types of funding. A discussion of these research incentives can be found in the companion policy paper on '*research and development for access to medicines*'.

Bibliography

- ⁱ Ten years in public health, 2007–2017: report by Dr Margaret Chan, Director-General, World Health Organization. Geneva: World Health Organization; 2017. Licence: CC BY-NC-SA 3.0 IGO.
- ⁱⁱ Morgan S, Bathula H, Moon S. Pricing of pharmaceuticals is becoming a major challenge for health systems. *BMJ*. 2020;:l4627.
- ⁱⁱⁱ Ward DJ, Doos L, Stevens A Trends in the costs of drugs launched in the UK between 1981 and 2015: an analysis of the launch price of drugs in five disease areas *BMJ Open* 2019;9:e027625. doi: 10.1136/bmjopen-2018-027625
- ^{iv} Dusetzina, S. B., "Drug Pricing Trends for Orally Administered Anticancer Medications Reimbursed by Commercial Health Plans, 2000-2014". *JAMA Oncology*. 2, 960–961 (2016).
- ^v EvaluatePharma. Orphan drug report 2017.4th ed. 2017. <http://info.evaluategroup.com/rs/607-YGS-364/images/EPOD17.pdf>
- ^{vi} Darrell M. West, John Villasenor, and Jake Schneider. "Private Sector Investment in Global Health R&D: Spending Levels, Barriers, and Opportunities" The Brookings Private Sector Global Health R&D Project, No. 2, September 2017, 10
- ^{vii} Moon S, Mariat S, Kamae I, Pedersen H. Defining the concept of fair pricing for medicines. *BMJ*. 2020;:l4726
- ^{viii} Moon S, Mariat S, Kamae I, Pedersen H. Defining the concept of fair pricing for medicines. *BMJ*. 2020;:l4726
- ^{ix} Gray A, Wirtz V, 't Hoen E, Reich M, Hogerzeil H. Essential medicines are still essential. *The Lancet*. 2015;386(10004):1601-1603.
- ^x Knowledgeportal.org. 2020 [cited 4 March 2020]. Available from: <https://www.knowledgeportal.org/affordability>
- ^{xi} Knowledgeportal.org. 2020 [cited 4 March 2020]. Available from: <https://www.knowledgeportal.org/affordability>
- ^{xii} Xu K, Evans DB, Kawabata K, Zeramdini R, Klavus J, Murray CJ. Household catastrophic health expenditure: a multicountry analysis. *Lancet* 2003;362:111-7. . doi:10.1016/S0140-6736(03)13861-5 pmid:12867110
- ^{xiii} World Health Organization (WHO) and World Bank Group. Tracking universal health coverage: first global monitoring report. 2015. https://www.who.int/healthinfo/universal_health_coverage/report/2015
- ^{xiv} <https://www.knowledgeportal.org/price-controls-regulation>
- ^{xv} Puig-Junoy J. Impact of European Pharmaceutical Price Regulation on Generic Price Competition. *PharmacoEconomics*. 2010;28(8):649-663.
- ^{xvi} Sood N, de Vries H, Gutierrez I, Lakdawalla D, Goldman D. The Effect Of Regulation On Pharmaceutical Revenues: Experience In Nineteen Countries. *Health Affairs*. 2008;27(Suppl1):w125-w137.
- ^{xvii} Kyle M. Pharmaceutical Price Controls and Entry Strategies. *Review of Economics and Statistics*. 2007;89(1):88-99.
- ^{xviii} Ferrario A, Dedet G, Humbert T, Vogler S, Suleman F, Pedersen H. Strategies to achieve fairer prices for generic and biosimilar medicines. *BMJ*. 2020;:l5444.
- ^{xix} Knowledgeportal.org. 2020 [cited 4 March 2020]. Available from: <https://www.knowledgeportal.org/price-controls-regulation>
- ^{xx} Plahte J. Tiered pricing of vaccines: a win-win-win situation, not a subsidy. *The Lancet Infectious Diseases*. 2005;5(1):58-63.

-
- ^{xxi} Knowledgeportal.org. 2020 [cited 4 March 2020]. Available from: <https://www.knowledgeportal.org/tiered-pricing>
- ^{xxii} Balasegaram M. Is tiered pricing the way for vaccines?. *The Lancet*. 2014;384(9946):852.
- ^{xxiii} Knowledgeportal.org. 2020 [cited 4 March 2020]. Available from: <https://www.knowledgeportal.org/health-technology-assessment>
- ^{xxiv} Morgan S, Bathula H, Moon S. Pricing of pharmaceuticals is becoming a major challenge for health systems. *BMJ*. 2020;:l4627.
- ^{xxv} Butler, M. S., Blaskovich, M. A. & Cooper, M. A. Antibiotics in the clinical pipeline in 2013. *J. Antibiot.* 66, 571–591 (2013)
- ^{xxvi} DiMasi J, Paquette C. The Economics of Follow-on Drug Research and Development. *PharmacoEconomics*. 2004;22(Supplement 2):1-14.
- ^{xxvii} Jones GH, Carrier MA, Silver RT, Kantarjian H. Strategies that delay or prevent the timely availability of affordable generic drugs in the United States. *Blood* 2016;127:1398-402. doi:10.1182/blood-2015-11-680058 pmid:26817958
- ^{xxviii} Rathod, S. K. (2010). Evergreening: A Status Check in Selected Countries. *Journal of Generic Medicines*, 7(3), 227–242. <https://doi.org/10.1057/jgm.2010.14>
- ^{xxix} Kapczynski A, Park C, Sampat B. Polymorphs and prodrugs and salts (oh my!): an empirical analysis of "secondary" pharmaceutical patents. *PLoS One*. 2012;7(12):e49470.
- ^{xxx} Morgan S, Bathula H, Moon S. Pricing of pharmaceuticals is becoming a major challenge for health systems. *BMJ*. 2020;:l4627.
- ^{xxxi} Hepatitis Australia (2016) Australia shows an alternative to rationing hepatitis C treatment [Online]. Available at: <https://www.hepatitisaustralia.com/newsarticles/australia-shows-an-alternative-to-rationing-hepatitis-c-treatment/8/6/2016> (Accessed: 14 December 2020)
- ^{xxxii} Lazonick, W. and Mazzucato, M. (2013) 'The risk-reward nexus in the innovation-inequality relationship: Who takes the risks? Who gets the rewards?' *Industrial and Corporate Change*, 22(4), pp. 1093–1128
- ^{xxxiii} Mary Anne Burke and Stephen A Matlin (eds.), *Global Forum for Health Research, Monitoring Financial Flows for Health Research* 2008.
- ^{xxxiv} Kneller R, "The importance of new companies for drug discovery: origins of a decade of new drugs". *Nature Reviews Drug Discovery*, 2010;9(11), 867-882.
- ^{xxxv} Morgan S, Bathula H, Moon S. Pricing of pharmaceuticals is becoming a major challenge for health systems. *BMJ*. 2020;:l4627.
- ^{xxxvi} Lopert R, Welch C. Costs of New Treatments for Hepatitis C Infection. *JAMA*. 2014;312(20):2168.
- ^{xxxvii} Année du médicament. (2015) New Drugs and Indications in 2014: Some advances this year, but many drugs are poorly evaluated, too expensive, or more dangerous than useful, *Rev Prescrire* 35 (376), pp. 132-136. English summary available online: *Prescrire International*. (2015), 24(159), 107-110. [Online]
- ^{xxxviii} 5. Colbert A, Rintoul A, Simão M, Hill S, Swaminathan S. Can affordability and innovation coexist for medicines?. *BMJ*. 2020;:l7058.
- ^{xxxix} Sarpatwari A, Avorn J, Kesselheim AS. State initiatives to control medication costs--can transparency legislation help? *N Engl J Med* 2016;374:2301-4. . doi:10.1056/NEJMp1605100 pmid:27305189
- ^{xl} United Nations Secretary-General's High-Level Panel on Access to Medicines. Report of the United Nations Secretary-General's High-Level Panel on Access to Medicines: Promoting innovation and access to health technologies. 2016. <http://www.unsgaccessmeds.org/final-report/>
- ^{xli} Moon S. Removing the blindfold on medicines pricing. *BMJ* 2018;360:k840. doi:10.1136/bmj.k840 pmid:29483091
- ^{xlii} Research and development costs | DNDi [Internet]. Drugs for Neglected Diseases initiative (DNDi). 2020 [cited 4 March 2020]. Available from: <https://www.dndi.org/about-dndi/costs/>
- ^{xliii} Colbert A, Rintoul A, Simão M, Hill S, Swaminathan S. Can affordability and innovation coexist for medicines?. *BMJ*. 2020;:l7058.
- ^{xliv} Cernuschi T, Gilchrist S, Hajizada A, Malhame M, Mariat S, Widmyer G. Price transparency is a step towards sustainable access in middle income countries. *BMJ*. 2020;:l5375.

-
- ^{xlv} Goldstein DA, Clark J, Tu Y, et al. A global comparison of the cost of patented cancer drugs in relation to global differences in wealth. *Oncotarget* 2017;8:71548-55. . doi:10.18632/oncotarget.17742 pmid:25775312
- ^{xlvi} Cernuschi T, Gilchrist S, Hajizada A, Malhame M, Mariat S, Widmyer G. Price transparency is a step towards sustainable access in middle income countries. *BMJ*. 2020;:l5375.
- ^{xlvii} Chhatwal J, Kanwal F, Roberts MS, Dunn MA. Cost-effectiveness and budget impact of hepatitis C virus treatment with sofosbuvir and ledipasvir in the United States. *Ann Intern Med* 2015;162:397-406. doi:10.7326/M14-1336 pmid:25775312
- ^{xlvi} Gilead Sciences fourth quarter and full year financial results. Gilead Sciences, Inc, 2019. <https://www.businesswire.com/news/home/20190204005678/en/Gilead-Sciences-Announces-Fourth-Quarter-Full-Year>
- ^{xlix} Garner S, Rintoul A, Hill SR. Value-based pricing: l'enfant terrible? *Pharmacoeconomics* 2018;36:5-6. . doi:10.1007/s40273-017-0567-4 pmid:29270834
- ^l Knowledgeportal.org. 2020 [cited 4 March 2020]. Available from: <https://www.knowledgeportal.org/mark-ups-taxes-supply-chain-costs>
- ^{li} Grabowski, Henry G. and John Vernon. "The Distribution of Sales Revenues from Pharmaceutical Innovation." *PharmacoEconomics* (2000): 21–32.
- ^{lii} World Trade Organization. 2018. Uruguay round agreement: TRIPS Article 27, Clause 1 [Online]. Available at: https://www.wto.org/english/docs_e/legal_e/27-trips_02_e.htm (Accessed 11 September 2018)
- ^{liii} Da7af2c8-d9b0-47a3-a3f6-89c3c3bfa02c.filesusr.com. 2020 [cited 4 March 2020]. Available from: https://da7af2c8-d9b0-47a3-a3f6-89c3c3bfa02c.filesusr.com/ugd/356854_a3278f7579fe41948f8286ec5caf9837.pdf
- ^{liv} Da7af2c8-d9b0-47a3-a3f6-89c3c3bfa02c.filesusr.com. 2020 [cited 4 March 2020]. Available from: https://da7af2c8-d9b0-47a3-a3f6-89c3c3bfa02c.filesusr.com/ugd/356854_a3278f7579fe41948f8286ec5caf9837.pdf
- ^{lv} Vondeling GT, Cao Q, Postma MJ, Rozenbaum MH. The impact of patent expiry on drug prices: a systematic literature review. *Appl Health Econ Health Policy* 2018;16:653-60. doi:10.1007/s40258-018-0406-6 pmid:30019138
- ^{lvi} Douglass CH, Pedrana A, Lazarus JV, et al. Pathways to ensure universal and affordable access to hepatitis C treatment. *BMC Med* 2018;16:175. doi:10.1186/s12916-018-1162-z pmid:30296935
- ^{lvii} Ferrario A, Dedet G, Humbert T, Vogler S, Suleman F, Pedersen H. Strategies to achieve fairer prices for generic and biosimilar medicines. *BMJ*. 2020;:l5444.
- ^{lviii} UCL Institute for Innovation and Public Purpose (2018) 'The people's prescription: Re-imagining health innovation to deliver public value', IIPP Policy Report, 2018-10. London: IIPP, Global Justice Now, Just Treatment, STOPAIDS. Available at: <https://www.ucl.ac.uk/bartlett/public-purpose/wp2018-10>
- ^{lix} Price Transparency In Medicine Faces Stiff Opposition - From Hospitals and Doctors. R. Bluth, KHN, Jul 2017. Accessed: Jan 2020. <https://khn.org/news/price-transparency-in-medicine-faces-stiff-opposition-from-hospitals-and-doctors/>
- ^{lx} Nicol D, Owoeye O. "Using TRIPS flexibilities to facilitate access to medicines" *Bull World Health Organ* 2013;91(7):533-539.
- ^{lxi} Saez C, "LDC Pharma IP Waiver Until 2033 Approved By WTO TRIPS Council," Intellectual Property Watch, 2015. URL: <http://www.ip-watch.org/2015/11/06/ldcpharma-ip-waiver-until-2033-approved-by-wto-trips-council/>
- ^{lxii} World Trade Organisation, "Compulsory licensing of pharmaceuticals and TRIPS," 2006. URL: https://www.wto.org/english/tratop_e/trips_e/public_health_faq_e.htm
- ^{lxiii} Raju 2017
- ^{lxiv} Nicol D, Owoeye O. "Using TRIPS flexibilities to facilitate access to medicines" *Bull World Health Organ* 2013;91(7):533-539.
- ^{lxv} Health Action International Europe (HAI Europe). Trading Away Access to Medicines Revisited. 2014. Available from: <http://haieurope.org/wpcontent/uploads/2014/09/Trading-Away-Access-toMedicines-Revisited.pdf>
- ^{lxvi} Da7af2c8-d9b0-47a3-a3f6-89c3c3bfa02c.filesusr.com. 2020 [cited 4 March 2020]. Available from: https://da7af2c8-d9b0-47a3-a3f6-89c3c3bfa02c.filesusr.com/ugd/356854_3f4f9251b88847d596cd085a88c4824f.pdf

^{lxvii} World Bank. 2018. Eliminating Hepatitis C from Egypt : 2017 update on current trends and policy recommendations - policy brief (English). Egypt's viral hepatitis program. Washington, D.C. : World Bank Group.

^{lxviii} Hepatitis Australia (2016) Australia shows an alternative to rationing hepatitis C treatment [Online]. Available at: <https://www.hepatitisaustralia.com/newsarticles/australia-shows-an-alternative-rationing-hepatitis-treatment/8/6/2016> (Accessed: 14 December 2018)

^{lxix} Health Action International. Policy options for promoting the use of generic medicines in low- and middle-income countries. 2016. Available from: http://haiweb.org/wpcontent/uploads/2017/02/HAI_Review_generics_policies_final.pdf

^{lxx} Knowledgeportal.org. 2020 [cited 4 March 2020]. Available from:

<https://www.knowledgeportal.org/patent-pools-ip>

^{lxxi} [Internet]. 2020 [cited 4 March 2020]. Available from: <https://unitaid.org/project/medicinespatent-pool/>

^{lxxii} [Internet]. Knowledgeportal.org. 2020 [cited 4 March 2020]. Available from:

<https://www.knowledgeportal.org/advanced-market-commitment>