



INTERNATIONAL GENERIC AND
BIOSIMILAR MEDICINES ASSOCIATION

IGBA recommendations for action to support a sustainable global pharmaceutical market for continued patient access worldwide to safe, effective and high-quality medicines

Generic and biosimilar medicines are critical to ensuring access to medicines around the world. However, for the benefits of these off-patent medicines to be captured by national health systems, governments must adopt policies that allow timely market access, while enabling prices that contribute to the sustainability of the generic and biosimilar medicines supply.

Moreover, there is a huge difference in healthcare systems around the globe. The calculation of the price of a medicine in a country should take into consideration the competitive environment, volume of consumption of the said product, potential economies of scale, the specific value of the medicine for the said country, the existence of reimbursement systems and other various market specificities. It is also important to recognize all relevant costs undertaken by the company, such as costs related to development, regulatory, quality assurance, serialization, environment risk assessment, pharmacovigilance, distribution and legal.

The sustainability of healthcare systems is debated daily by stakeholders around the world. Challenges such as the high cost of new originator medicines, drug shortages, limited access to medicines, lack of universal health coverage (UHC), and the sustainability of generic and biosimilar medicines industries are issues impacting all stakeholders. IGBA's mission is to promote solutions to these challenges while continuing to advance the widest possible patient access to safe, effective and high-quality medicines around the world. Our industries consequently play a key role for millions of patients and thereby contribute to the 2030 UN Member States sustainable development

About IGBA

The International Generic and Biosimilar medicines Association (IGBA) was founded to strengthen cooperation between associations representing manufacturers of generic and biosimilar medicines from around the world. The IGBA is at the forefront of preserving sustainable competition within our industry, by stimulating competitiveness and innovation in the pharmaceutical sector; thereby, ensuring millions of patients around the world have access to high quality, pro-competitive medicines. For more details, regarding IGBA and its member associations, see the IGBA website at: www.igbamedicines.org.

goals, including achieving universal health coverage (UHC) and access to safe, effective, quality and affordable essential medicines for all¹.

The data below shows the positive impact that generic and biosimilar medicines have on patients and health systems in the regions covered by our membership:

- In Australia, the genericised medicine market accounts for just over 84% of the volume of subsidised medicines but only 28.7% of the cost. During the period from 2016 to 2019, the reimbursed script rate by volume increased by 7%, the cost fell by 12%. This demonstrates the significant savings that generics have provided to the Pharmaceutical Benefits Scheme (PBS). Furthermore, in 2018, 7 of the top 10 subsidised medicines by value were biological medicines. This highlights the emerging importance of biosimilar introduction and uptake in Australia to ensure sustainability of the Australian PBS and broader healthcare sector.
10 biosimilars have been approved so far by the Therapeutic Goods Administration (TGA) in Australia (status October 2019).
- In Canada for 12 months ending June 2019, generic drugs were dispensed to fill 72.8% of retail prescriptions, or 530 million prescriptions. Growth of generic prescriptions was 6.1% compared to the previous year. Sales of generic pharmaceuticals accounted for only 19.5% of the total cost of Canada's total annual prescription drug expenditure of 29.6 billion dollars.
17 biosimilars were approved by Health Canada (September 2019).
- In Europe, almost 50 million people are taking generic medicines every day for hypertension and in 2017 there were over 700 million patient days of clinical experience with biosimilar medicines. Generic medicines have doubled access to therapy for hypertension, diabetes, cardiovascular, epilepsy and mental health over 10 years in Europe (2007-2017). Currently generic medicines account for 67% of dispensed medicines and 29% of pharmaceutical expenditure at list prices. More importantly, generic and biosimilar medicines have doubled access to therapy which was previously restricted due to the absence of price competition on the market. Without generic medicines competition, patients and healthcare systems would have paid €100 billion more for their drugs bill.
Biosimilar medicines have increased access by up to 250% in different EU countries and therapy areas. The potential to increase access to biological therapies is massive over the next few years especially for immune disorders and cancer.

¹ Goal 3: ensure healthy lives and promote well-being for all at all ages <https://bit.ly/2KupAJ0>

54 biosimilars have been approved so far by the European Commission for the European Economic Area (EEA) markets (status September 2019).

- In India, 95% of all prescribed medicines are branded generics, which contributes substantially to patient access and expenditure savings. For example, generic versions of the cancer medications paclitaxel, docetaxel, gemcitabine, oxaliplatin and irinotecan generated an estimated savings of about ₹ 47 billion (US\$ 843 million) in 2012². India is also the largest provider of generic drugs globally. The Indian pharmaceutical industry supplies over 60 per cent of global demand for various vaccines & ARV drug supplies, 30% of UNICEF's annual supply globally and about 60%-80% of the UN purchases of drugs. India contributes approximately 57% of Active Pharmaceutical Ingredients (APIs) and 69% Finished Pharmaceutical Products (FPP) to the Pre-Qualified list of WHO. Indian generics manufacturers also play a critical role in bringing new safe, affordable drugs to US consumers. The Indian industry received 207 ANDA FDA approvals out of a total of 476 (43%) in the first half of 2019 and consequently contributes to billions of savings in the U.S.A.
- In Japan, the share volume of generic medicines is increasing every year and the rate of generic sharing as of September 2018 is around 73% of the substitutable market. This was an increase of the share by 6.8 % compared to the previous year. The saving in drug expenditure in the fiscal year of 2018 is estimated to amount to 1.4 trillion JPY (= US \$12.1 billion).

18 biosimilars have been approved in Japan so far by the Pharmaceutical and Medical Devices Agency (PMDA) Japan (status June 2019).

- In Jordan, generics, branded generics and biosimilars account for about 83% by volume and 38% by value of the medicines dispensed in the public health institutions. Access to medicines in Jordan has significantly improved with the introduction of generic and biosimilar products for oncology and inflammatory diseases.

11 biosimilars have been approved by Jordan Food & Drug Administration (JFDA) (as of September 2019).

- In Malaysia for 2018, the share of generic medicines constituted 69% of the total pharmaceutical supply with 28% of total pharmaceutical sales by value. The supply of larger quantities at lower value highlights the important contribution of this sector in providing access to medicines to the public.

² WHO Information session for Member States and Non-State Actors in official relations: Technical report on pricing of cancer medicines and its impacts. 25.4.2019

9 biosimilars have been approved by the Malaysian Drug Control Authority as of 1st August 2019.

- The total market of South Africa is about 3.4 billion Euros. Across both State and Private sectors, generic medicines have a volume market share of 69.6%. By value, this market share is 47.5% or 1.6 billion Euro, which indicates the high pricing of the originator products. Two biosimilars (filgrastim and Trastuzumab) have been approved so far by the South African Health Products Regulatory Agency (SAHPRA) (status September 2019).

There are approximately 40 Biosimilars which have been submitted for registration.

- In Taiwan, generic medicines account for about 80% of dispensed medicines but only 28% of the total annual drug expenditure in 2017.
- In the U.S.A, generic drugs have saved nearly \$2 trillion in the last decade, generating \$293 billion in savings in 2018 alone. Medicare and Medicaid savings amounted to \$137 billion last year, \$2,254 per Medicare enrollee and \$817 per Medicaid enrollee. Generics account for 90% of prescriptions dispensed but only 22% of total drug costs in the U.S.

23 biosimilars have been approved by the U.S. Food and Drug Administration (FDA) and 9 launched so far (status September 2019).

For nearly 35 years, the availability of affordable, FDA-approved generic medicines has meant greater access to life-saving treatments for millions of patients. Generics have delivered trillions of dollars in savings for employers, health plans, state and federal governments and, most importantly, patients. And the development of biosimilar medicines and complex generics means the availability of innovative specialty and biologic treatments for patients at lower prices. This is the result of the commitment of generic and biosimilar manufacturers to improving patients' lives through timely access to affordable medications.

But strong headwinds threaten generic and biosimilar competition. Without action to ensure a sustainable, competitive environment for manufacturers of affordable medicines. America's patients will continue to face increasingly high brand drug prices.

The above-mentioned data represent the benefit that generic and biosimilar medicines are bringing to patients while supporting the long- term sustainability of healthcare systems in countries around the world.

To be able to continue to play this crucial role and given the growing concerns about the availability of essential generic medicines and the risk of shortages, challenges for the medium and long-term

sustainability of the generic and biosimilar medicines industries must be addressed, in order to ensure the best possible solutions for patients and healthcare systems.

The role of generic and biosimilar medicines in sustainable healthcare systems

Over the past several years, mandatory price cuts on generic medicines have been strongly applied in almost all regulated markets with government-financed health systems, while prices of new chemical entities have increased significantly. For example, in Europe, generic medicines only contribute 2-3% of the total healthcare budget, so cutting their prices has a limited financial impact but this can have a major impact on the supply of essential first line medicines for public health.

Price cuts in several European countries, for example, have also led to unsustainable business dynamics, the withdrawal of medicines from the market and ultimately to shortages of these medicines. For example, Greece and Romania have introduced numerous price cutting measures (external reference pricing, mandatory rebates and clawback taxes) to generic medicines which has led to the withdrawal of many products and to a limited generic penetration rate. Consequently, patients in these countries need to rely on more expensive reference products for their essential medicines supply.

Rather than cutting prices of generic medicines, healthcare policies should stimulate their uptake in order to take advantage of the efficiency that these products generate through organic price reductions stemming from market competition. The generic and biosimilar medicines sectors are the main drivers of sustainable pharmaceutical spending by reducing the cost of off-patent medicines through competition. A major challenge facing health systems is how to incentivize sustainable competition to specialty markets where the investment costs and the risks are much higher than conventional small-molecule generic medicines. Competition from biosimilar medicines in the EU-US markets could result in savings of \$100 billion/year. This is more than the combined EU-US generic medicines market at current prices. Governments have much more to gain if they shift their focus away from cost containment on already inexpensive generic medicines to removing barriers to competition in specialty markets such as biological medicines.

Consequently, governments and payers/insurers must recognize that current policies and practices in many markets threaten the viability of the generic and biosimilar business model, and thus the long-term sustainability of the off-patent industry and all the benefits generated for patients and healthcare systems. Market dynamics that limit the ability of generic and biosimilar medicines to

remain viable, whether through artificially low prices or limited market uptake, could result in lack of future competition and the perpetuation of costly monopolies for originator medicines.

The generic medicines industry cannot follow a “cost of goods plus” (cost-plus) model in a competitive market as there are multiple factors (as described below) that must be paid for through an effective pricing system. There is a dynamic aspect to generic medicines competition. Generic companies typically earn their returns at launch by taking market share from originator companies through price competition. Price erosion is highest at this phase of market entry (50% to reference price according to the Sector Inquiry by the European Union Competition authority³). At a second phase, generic competition leads to more price competition between generic manufacturers. As prices reach very low levels over time, the number of manufacturers decline, and prices tend to stabilize. If prices fall too low due to government cost-containment measures, markets become overly reliant on one or two manufacturers or to consolidation of the manufacturing supply chain (limited number of API suppliers). This increases the risk supply stock outs and increasingly to shortages. In Europe, this issue has been recognised as a problem and the recent Euripid guidance has recommended that countries not apply external reference pricing to generic medicines⁴. The Australian Government, for example, has recognised the link between the price paid for generic medicines and their ongoing supply. Through discussions under a Strategy Agreement between the Australian Government and the Australian Generic and Biosimilar Medicines Association, an analysis was conducted by the Department of Health, looking at a selection of generic medicines including a number on the WHO Essential Medicines List (EML). To support the ongoing supply of medicines to Australian patients, price increases were applied to around 60 medicines in December 2016. These examples show that competition from generic medicines can dramatically reduce prices at loss of exclusivity of the reference molecule and that competition between generic manufacturers can further reduce prices. However, if prices are reduced to unsustainable levels due to government measures, there is a risk of supply availability problems.

As mentioned above, a “cost-plus” pricing model will not render a fair price to generic manufacturers for the costs associated with developing, manufacturing, launching, selling and

³ EU pharmaceutical sector inquiry, Final Report. p.85
<https://bit.ly/2MBCKH7>

⁴ Guidance document on External Reference Pricing (ERP)
<https://bit.ly/2Sdvr9N>

maintaining a continuous supply of that medicine. When considering the cost of medicines, it is important to recognize all relevant costs undertaken by the company, including:

Development costs:

The development of a new generic medicine involves several bioequivalence trials. These trials together with formulation development, analytical method development, stability studies, etc. are an important contributor to the total cost of a generic product. Today, as there is no scientific and regulatory framework supporting global development for generic medicines, companies are consequently required to conduct multiple trials to meet different national requirements. For example, for a generic medicine approved in the EU, additional and different data is required to be approved in, for example, the United States, Switzerland, Japan or South Africa. The IGBA therefore highly welcomes the announcement by the ICH on harmonizing standards for generic medicines which are key for reliance in the future. For the first time ever, generic medicines will have a new focus within the ICH. We see this as a recognition by the ICH Assembly of the importance of generic medicines in healthcare and the value of harmonization of technical standards to guarantee access to high quality generic medicines to patients worldwide. ICH is indeed uniquely positioned to develop these global standards for generics given the ICH reforms in 2015 establishing it as the global venue for harmonization of standards for all pharmaceutical products.

Regulatory costs:

The marketing of a generic product can only be accomplished after the submission and approval of a Marketing Authorization Application (MAA) dossier to the relevant competent authority. The establishment of such a dossier is very resource intensive, particularly in highly-regulated markets. Furthermore, there are differences in regulatory standards globally. Navigating this global patchwork of regulation has a significant impact on the cost of manufacturing, dossier submission, post-marketing surveillance, *etc.* Moreover, after the approval of the MAA dossier, the marketing authorization must be maintained, an activity that involves the submission of numerous variations and renewals which contributes significantly to costs required to keep the product on the market, while government policies have introduced price cuts. For example, in Europe alone, the number of variations has increased by 75% over the last 10 years. Highly regulated markets have significantly higher maintenance costs than less regulated markets.

In addition, manufacturers increasingly face costs associated with other government mandated programs. For example, in Europe, the falsified medicines directive has cost manufacturers at least over €1 billion to upgrade manufacturing lines with barcode printers and they have been confronted with more complex manufacturing logistics that have slowed production speed by 15-25%. In the US, the GDUFA I fees (2013 – 2017) were \$300 million/year (inflation adjusted year over year), and now, under GDUFA II (2018 – 2022) fees are \$493 million/year (inflation adjusted year over year).

Any manufacturers selling medicines in these highly regulated markets will bear the cost of these increasing regulatory requirements regardless of manufacturing location.

Quality Assurance (QA) costs:

The pharmaceutical industry is a globalized industry that relies on supply chains that span multiple countries and are often very complex. To keep oversight of these supply chains and to guarantee the quality of the products manufactured throughout the supply chain, global QA and global auditing of the various supply chains is very important and contributes to costs.

Serialization and Environment Risk Assessment costs

The serialization requirements of the European Falsified Medicines Directive (FMD) required an investment of more than €1 billion and IT system costs of over €100 million/year. Draft reforms to environment risk assessments (ERAs) for pharmaceuticals in the EU could deter generic launches and reduce competition since costs of up to € 1.0 million per product for conducting ERAs would impose a considerable burden on the European generic medicines industry. While these are European examples, many countries are considering regulation against falsified medicines or the environment. As more countries adopt such measures, manufacturers will need to make similar investments over the next few years⁵.

Pharmacovigilance Costs:

Pharmacovigilance regulations in markets around the world are becoming more arduous and stringent, requiring generic and biosimilar companies to hire more costly skilled staff and purchase

⁵ The US, Russia and Saudi Arabia are all in the process of establishing serialisation requirements. The WHO is launching work to harmonise serialisation requirements globally and is considering the possibility of serialisation for less regulated markets to reduce the risk of falsified medicines. The WHO has launched a consultation on applying environmental manufacturing regulations globally, but no decision has yet been taken on this matter.

and/or develop complex IT systems. Dossiers must be maintained and updated to further promote patient safety, adding additional costs.

Distribution costs:

The regulations relating to supply chain management are becoming more laborious and rigid, and consequently more costly. Authorities are imposing more stringent conditions on manufacturers to ensure patient safety. For example, the EU generic medicines companies are facing huge costs related to the implementation of the anti-counterfeiting provisions of the EU's Falsified Medicines Directive (FMD). Anti-tampering devices and 2-D data matrices on packs became mandatory for all prescription and some non-prescription medicines. The industry-funded system has required an investment of over €1 billion from manufacturers to update production and packaging lines and will require €100-200 million annually to maintain the information-technology (IT) structure.

Legal costs:

In a highly competitive pharmaceutical market, it is very rare for a generic company to enter the market without undertaking litigation – or defending themselves from litigation (usually patent issues) before courts. Especially for the generic sector, these costs are particularly relevant and represent a significant burden.

Cost of capital:

In basic terms, cost of capital is the return on funds to investors, both shareholders and lenders expecting a reward for their investment. Without profit expectations very little investment would be applied to pharmaceutical manufacturing.

Many of the above cost categories also apply to **biosimilar medicines**, with even greater financial requirements than for generic medicines. Development of a biosimilar medicine can take nearly a decade and \$300 million for a single product, based on time to approval alone. A large part of this cost is driven by current regulatory requirements for confirmatory clinical trials and use of locally-authorized reference products for comparability demonstration. Even if the biosimilar medicine is the same product and has been developed for the global market, most jurisdictions require a unique regulatory application, sometimes with different data requirements. The cost associated with

satisfying various regulatory requirements globally is substantial, particularly when clinical studies are involved. In addition to substantial costs associated with development and approval, biosimilar medicine companies typically bear extensive legal costs related to patent litigation, which can delay market launch for years in some jurisdictions.

Once a biosimilar medicine can be launched in a market, there are many more costs associated with achieving market uptake and successful utilization. Some of these costs are analogous to those required for generic medicines, such as quality assurance, distribution and pharmacovigilance, but some are more in line with investments associated with originator biological products, such as patient assistance programs, physician education and dedicated sales teams. These costs are not required in all markets, such as those with smaller government-financed health systems having greater ability to mandate biosimilar uptake through national procurement, but in some markets these brand-style investments are a necessity to compete and obtain market share from the originator biological medicine.

Furthermore, because biological medicines constitute some of the most lucrative products globally, some originator biologic companies are unwilling to let their market share convert easily to biosimilar medicines, and successfully engage in tactics to prevent biosimilar competition. Some of these tactics are under review by competition authorities in various countries. A major threat to biosimilar competition is a tactic where the originator biologic company undercuts the biosimilar price to retain market share. While some payers see this reduction in originator price as a welcome result of competition and find no issue with continuing to prefer the lowest-cost alternative, even if that is the originator biologic, this tactic is a fundamental barrier to biosimilar competition that will result in the inability of companies to bring future biosimilar medicines to the market. Originator biologic companies have enjoyed monopolies for years, sometimes decades, and have the financial flexibility to undercut biosimilar competition, happily taking short-term price cuts knowing that future monopolies will be free from biosimilar competition should the market prove unviable for biosimilar medicines.

Consideration of the unique market dynamics of biosimilar medicines is critical in establishing policies that support sustainable healthcare systems. While biosimilar medicines are a form of off-patent competition, like generic medicines, the development, approval, legal and commercialization costs far exceed those of generic medicines and are particularly susceptible to originator tactics to impede competition. Government recognition of these unique dynamics and efforts to address the

challenges facing biosimilar medicines is fundamental to ensuring ongoing competition and access to biological medicines.

If a comparison between cost and price is to be made, we recognize that this is a complex exercise, but it is critical that all the above aspects be taken into consideration.

Moreover, there is a huge difference in healthcare systems around the globe. The calculation of the price of a medicine in a country should also take into consideration the competitive environment, volume of consumption of the said product, potential economies of scale, the specific value of the medicine for the said country, the existence of reimbursement systems and other various market specificities. The price of a pharmaceutical product cannot be taken as an absolute number as in many instances it is very challenging to accurately determine.

General recommendations towards a sustainable health care system

In addition to the recommendations above supporting the sustainability of the generic and biosimilar supply, the IGBA would like to put forward key additional recommendations deemed relevant to optimize costs of medicines and to support sustainable health care systems:

- Stimulating generic and biosimilar medicines competition via national uptake measures and removal of market barriers, allowing competition to start on day 1 after patent expiry
- Ensuring balanced Intellectual Property /regulatory incentives that reward and encourage generic and biosimilar market entry
- Stressing the importance of stringent patent examination and quality of patents more generally to reduce frivolous litigation
- Advancing regulatory frameworks supporting true global development of generic, complex generic and biosimilar medicines
- Converging and simplifying registration and marketing authorization maintenance requirements by Medicines Regulatory Authorities
- Avoiding duplicative regulatory activities with no added value for patients and science by sharing of information between National Regulatory Authorities (NRAs), necessary for regulatory reliance and recognition mechanisms leading to faster approvals and post-approval changes and hence availability of medicines worldwide
- Supporting mutual recognition of Good Manufacturing Practice (GMP) inspections

- Ensuring that trade agreements do not undermine the balance between the originator pharmaceutical and generic/biosimilar medicine industries. FTA pharmaceutical provisions should not be used to support originator evergreening strategies that undermine access to medicines⁶.

IGBA remains ready to cooperate constructively with all the relevant actors in order to increase access to high quality medicines and enable better healthcare outcomes globally.

15.10.2019

⁶ IGBA Trade Principles: generic and biosimilar medicines
<https://bit.ly/318F6T0>