

Special Issue Article "Generic Drugs"

Mini Review

Generic Drugs — Essential for the Sustainability of Healthcare Systems with Numerous Strategies to Enhance their Use

Brian Godman^{1,2,3*}, Amos Massele⁴, Joseph Fadare^{5,6}, Hye-Young Kwon⁷, Amanj Kurdi^{1,2,8}, Francis Kalemeera⁹, Shahzad Hussain¹⁰, Alice Pisana¹¹ and Johanna C Meyer²

¹Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, UK

²Division of Public Health Pharmacy and Management, School of Pharmacy, Sefako Makgatho Health Sciences University, Pretoria, South Africa ³School of Pharmaceutical Sciences, Universiti Sains Malaysia, Malaysia

⁴Hurbert Kairuki Memorial University, Tanzania

⁵Department of Pharmacology and Therapeutics, Ekiti State University, Nigeria

⁶Department of Medicine, Ekiti State University Teaching Hospital, Nigeria

⁷Division of Biology and Public Health, Mokwon University, Korea

⁸Department of Pharmacology, College of Pharmacy, Hawler Medical University, Iraq

⁹School of Pharmacy, University of Namibia, Namibia

¹⁰National Institute of Health, Islamabad, Pakistan

¹¹Department of Global Public Health, Karolinska Institutet, Sweden

ARTICLE INFO

Received Date:June 03, 2022Accepted Date:June 27, 2022Published Date:June 30, 2022

KEYWORDS

Generic drug; Venlafaxine; Angiotensin

Copyright: © 2022 Brian Godman et al., Pharmaceutical Sciences And Biomedical Analysis Journal. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Citation for this article: Brian Godman, Amos Massele, Joseph Fadare, Hye-Young Kwon, Amanj Kurdi, Francis Kalemeera, Shahzad Hussain, Alice Pisana and Johanna C Meyer. Generic Drugs – Essential for the Sustainability of Healthcare Systems with Numerous Strategies to Enhance their Use. Pharmaceutical Sciences And Biomedical Analysis Journal. 2022; 4(1):126

Corresponding author:

Brian Godman,

Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow G4 ORE, United Kingdom,

Email: Brian.godman@strath.ac.uk

ABSTRACT

The increasing use of lower-cost multiple sourced medicines (generics) and biosimilars are essential to attain or retain universal healthcare in the face of continual pressure on available resources. Alongside this, reduce patient co-payments and enhance access to medicines in countries with high co-payments where affordability is an issue. Supply-side measures, including aggressive procurement practices and increased transparency in the manufacture and pricing of generics, can appreciably lower the price of generics. Such measures alongside demand-side measures can enhance savings versus originators as well as increase access to standard medicines. However, there needs to be trust in the generics to maximise savings. The same applies to biosimilars. Multiple demand-side measures can also appreciably enhance the preferential prescribing of multiple sourced medicines versus still patented medicines in a class or related class without compromising care. As a result, enhance utilisation at lower costs. Countries can learn from each other when planning or instigating reforms, and this will grow.

INTRODUCTION

We have seen global expenditure on medicines rising appreciably in recent years with estimates that expenditure will reach US\$1.5 trillion globally by 2023 [1]. This growth in medicine expenditure represents an annual compounded growth rate of 3–6% (1), driven by many factors [2]. Key factors include the growing prevalence of Non-Communicable Chronic Diseases (NCDs), which include Coronary Vascular Disease (CVD) and diabetes, along with an associated increase in medicine use, increasing prices and expenditure on new medicines especially for orphan diseases and oncology, as well as changes in guidelines and clinical practice [3-9]. This increase in expenditure on medicines has ramifications for the sustainability of universal





SCIENTIFIC LITERATURE

healthcare in high-income countries, which have resulted in calls for new approaches to the pricing of new medicines [7,8,10,11]. Alongside this, concerns with the management of diseases among Lower- and Middle-Income Countries (LMICs) where expenditure on medicines can be as high as 60% of total healthcare expenditure [12,13]. In certain disease areas such as diabetes and associated complications, expenditure on medicines can be as high 90% of total costs [9,14,15]. An appreciable proportion of expenditure on medicines will be out-of-pocket in many of these countries with potentially catastrophic consequences on families when members become ill [12,16-18]. Consequently, the medicines' budget must be carefully managed with initiatives introduced to achieve sustainable development goals especially for NCDs [2,19,20].

One of the key initiatives to make savings available to fund increased volumes of medicines, enhance the affordability of medicines to patients, as well as fund new premium priced medicines to address unmet need, is through increased prescribing of multiple sourced medicines (generics) and biosimilars [4,21-25]. This includes encouraging the preferential prescribing of multiple sourced medicines versus originators as well as against still patented medicines in the class or related class without compromising care [4]. Numerous publications have demonstrated similar effectiveness and safety between originator and generic medicines provided bioequivalence has been demonstrated [26-32]. Consequently, patient care should not be compromised. However, there can be concerns where there are no strict regulations or enforcement surrounding the quality of generics within a country impacting on both physician and patient acceptance of generics, which is a major challenge in LMICs [33-36]. This needs to be addressed to enhance their use including strengthening healthcare systems [37].

Initiatives to enhance the prescribing and dispensing of generic medicines versus originators include voluntary or compulsory International Non-Proprietary Name (INN) prescribing coupled with education of key stakeholder groups, compulsory substitution, and/ or incentives to pharmacists to increase substitution [4,25,38,39]. This is apart from an agreed limited number of clinical situations where INN prescribing or compulsory substitution may cause concern. Disease areas and medicines of concern include long-acting calcium channel blockers and certain medicines for patients with epilepsy [40-

43]. There have also been concerns with switching between originator and generic medicines in patients prescribed immunosuppressants following transplantation; however, this now appears to be less of an issue [44].

High voluntary INN prescribing rates in the United Kingdom, which can be up to 99% or more of prescription items dispensed in non-controversial clinical situations, are achieved by education and clinical practice starting in medical schools and continuing post-qualification via electronic reminders and other approaches [45-47]. High utilisation of generics in Sweden versus originators have been achieved by physician and patient acceptance of the regulations surrounding compulsory generic substitution apart from the limited number of disease areas or molecules where the Swedish Medicines Agency has concerns. In addition, patients having to cover the additional costs themselves if they still prefer an originator versus a generic [40,48]. This is reflected for instance by generic losartan and generic venlafaxine accounting for 97% to 99.6% of total losartan and venlafaxine respectively soon after their availability [49,50].

One potential advantage of INN prescribing is that possible confusion with different product names in the case of different names for each branded generic and the originator can be addressed by just having the INN name on packages of generic medicines. This is the situation in the United Kingdom, which is different to a number of European and other countries [2]. Different names on the packages of the same medicine can cause confusion among patients especially if different named medicines are being dispensed each time as a result of procurement and other practices [2]. The resultant confusion can potentially result in over- or under-dosing unless the dispensing pharmacist and/ or prescribing physician spends time with patients re-assuring them that the medicines are the same [51-53]. As mentioned though, there can be concerns with the quality of generics among LMICs challenging routine INN prescribing [33,34,54,55]. The World Health Organisation (WHO) pre-qualification scheme is one avenue for ensuring the quality of generic medicines among LMICs [56]. This scheme has been successful in helping to promote access to artemisin-based antimalarial therapies in many countries; however, there are still issues with the quality of multiple sourced medicines including among African countries because of issues with the

Generic Drugs – Essential for the Sustainability of Healthcare Systems with Numerous Strategies to Enhance their Use. Pharmaceutical Sciences And Biomedical Analysis Journal. 2022; 4(1):126.



SCIENTIFIC LITERATURE

regulatory and market environment in some of these countries [57]. The Lomé initiative that has recently been launched in Africa to address falsified and substandard medicines is a major step forward to enhance patient and physician trust in generic medicines where there are concerns, building on earlier WHO initiatives [58-60]. We will continue to monitor these initiatives in view of their importance for patients.

There can be situations where companies try and influence the prescribing of generics as seen when Sanofi in France had concerns with generic clopidogrel [61,62]. Eventually though the Company were fined by the French health authorities for the level of misinformation [62]. We have also seen Companies threatening physicians with legal action in the UK if they prescribe medicines by their INN name rather than brand name for still patented indications [63]. However, this does not appear to be the case for generic cancer medicines in the UK, which is welcomed given ever increasing expenditures on oncology medicines [64].

The instigation of supply-side measures among countries has resulted in prices for generics becoming as low as 2% to 4% of pre-patent loss prices, which include medicines for NCDs and oncology [64,65]. Measures include regular procurement auctions in the Netherlands, compulsory generic substitution coupled with regular auctions in Sweden as well as increasing transparency in the manufacture and pricing of generics in the United Kingdom [45,47,49,66]. Increased transparency in the pricing of generics helped to reduce their costs by alleviating practices whereby generic companies sought to keep prices high and offer discounts to pharmacists to preferentially dispense their generics, which have been common in some countries despite legislation [47,67]. However, there are concerns that if the price of generics becomes too low, this will make their manufacture unprofitable. As a result, leading potentially to shortages; alternatively, other manufacturers becoming the new license holders appreciably increasing their price [64,68,69]. Low prices for generics are though not universal. Prices of generics typically depend on the regulations within a country [64]. As a result, there can be appreciable differences in the prices of generics among countries as seen in the case of prices for oral multiple sourced oncology medicines across Europe, with generally population sizes having limited impact on reimbursed prices despite earlier concerns [64,70].

We have seen situations where initiatives among countries to increase the prescribing and dispensing of generics have not achieved the desired result. Whilst the health authorities in Abu Dhabi sought to conserve resources by introducing compulsory INN prescribing, there were no simultaneous measures to encourage pharmacists to preferentially dispense the cheapest multiple sourced medicine. Alongside this, the authorities did not instigate any demand-side measures to encourage physicians to preferentially prescribe multiple sourced products first line as opposed to patented medicines in a class when care is not compromised. As a result, the desired savings were not achieved exacerbated by the manufacturers of patented medicines encouraging their preferential prescribing by questioning the quality of generics [71]. In South Korea, the Government introduced policies to try and increase pricing competition among generics and originators to increase savings from generic availability. However, the ratio of originator to generic prescribing actually increased without any concomitant demand-side measures physicians to encouraae to preferentially prescribe multiple-sourced medicines [72]. Consequently, well thought out and complimentary measures are typically more likely to achieve desired outcomes than complex disparate measures [72,73].

We have also seen that multiple demand-side measures are typically needed to encourage the preferential prescribing of multiple-sourced medicines in a class or related class versus patent-protected medicines. Multiple demand-side measures in Sweden, which included physician education, prescribing targets and financial incentives, encouraged the preferential prescribing of generic omeprazole and generic simvastatin versus patented medicines in their classes when these first became available. These multiple demand-side measures, coupled with aggressive measures to lower the prices of generics in Sweden [74,75], produced considerable savings when compared with Ireland with more its limited demand-side measures [75,76]. In both countries, there was an appreciable increase in the prescribing of statins and Proton Pump Inhibitors (PPIs), with the increase in statin prescribing driven by increasing rates of coronary vascular disease and a greater understanding of their patient benefits [77,78]. However, expenditure for PPIs and statins was over ten times higher in Ireland in 2007 when adjusted for population size [75].



SCIENTIFIC LITERATURE

Low prices for generics in Scotland, coupled with multiple demand-side measures to preferentially prescribe multiple sourced medicines, have also resulted in appreciable savings alongside improvements in the quality of care [46,79]. In the case of lipid-lowering therapies, this meant initiatives to increase the dose of statins prescribed as more data became available demonstrating improved outcomes at higher doses [46,77]. These multiple measures resulted in a 50% reduction in expenditure on lipid-lowering therapies in Scotland between 2001 and 2015 despite a 412% increase in their utilization [46]. Similarly, total expenditure on PPIs fell by 66.7% in 2017 compared with 2001 despite a 3.06-fold increase in their utilization [79].

We have seen a similar situation regarding the impact of initiatives to encourage the preferential prescribing of generic Angiotensin Converting Enzyme Inhibitors (ACEIs) versus patented Angiotensin Receptor Blockers (ARBs) without compromising care. The instigation of prescribing restrictions for ARBs in Austria and Croatia, as well as multiple measures in Scotland to encourage the preferential prescribing of ACEIs including again physician education, prescribing targets and financial incentives, appreciably limited the prescribing of ARBs in these countries compared with Portugal with its limited demand-side measures [45,80]. As a result, expenditure on renin-angiotensin inhibitors was 2.4 times greater in Portugal in 2007 when adjusted for population size versus Scotland despite similar increases in utilisation of these medicines between 2001 and 2007 [45,80]. Of note was that the greater follow-up of prescribing restrictions by the authorities in Croatia versus Austria among GPs, which included access to patients' histories with the potential fines for physicians if abuse was suspected, resulted in more limited prescribing of ARBs in Croatia [45,80]. Encouragingly, the multiple demand-side measures introduced in Scotland appeared to be as effective with limiting ARB prescribing compared with the prescribing restrictions in Austria and Croatia [45]. This is important for countries that are unable to introduce prescribing restrictions as a potential demand-side measure to enhance the preferential prescribing of multiple sourced medicines versus patented medicines [2].

There was again appreciably variation among European countries regarding the extent of demand-side measures

introduced to enhance the prescribing of losartan as the first ARB to lose its patent without compromising care [81]. The removal of patented ARBs from the reimbursement list in Denmark had the greatest impact, with the utilisation of losartan rapidly reaching 92.3% of total ARBs [82]. Multiple demand-side measures in Sweden including education, prescribing targets, switching and financial incentives, resulted in losartan rapidly reaching 37.6% of total losartan utilisation [50]. Lifting prescribing restrictions for losartan but not for other patented ARBs resulted in its increased prescribing in Austria and Belgium following generic availability; however, the extent of the increase was more limited compared with the multiple demand-side measures in Sweden and the delisting of patented ARBs in Denmark [81,83,84].

No specific demand-side measures were introduced in Scotland to enhance the prescribing of losartan first line versus still patented ARBs since the authorities believed other quality targets were more important and they did not want to overload physicians which resulted in little change in physician prescribing habits post generic losartan [85]. Alongside this, losartan was already the most prescribed ARB in Scotland and there was a belief that there could be mixed messaging away from just encouraging the preferential prescribing of ACEIs first line, which had been very successful in Scotland [45,85]. However, one regional primary care group in England instigated multiple measures to enhance the prescribing of losartan versus patented ARBs to necessarily save costs without compromising care [52]. Losartan rapidly accounted for 65% of all ARBs dispensed, up from 24% pre the initiatives, with total ARB expenditure 59% below pre-study levels [52]. Overall, annual net savings in this primary care group were estimated at over eight-times the cost of implementing these multiple measures [52] providing direction to others. These various studies demonstrate that multiple measures are typically needed to successfully change prescribing habits [4]. Without such measures, which typically means passive activities among health authorities, there can be limited change in prescribing habits as seen with losartan prescribing in Scotland [85]. We also saw this with limited impact of additional quality targets for the prescribing of ACEIs over ARBs in the UK with no appreciable broadcasting of these increased targets nor additional financial incentives [86].



SCIENTIFIC LITERATURE

We see a similar situation with respect to the impact of demand-side measures to enhance appropriate utilisation of antibiotics. The authorities in Azerbaijan, the Republic of Srpska, and Slovenia, successfully introduced multiple measures over a number of years to reduce inappropriate prescribing and dispensing of antibiotics, as well as limit increases where utilisation rates were already low, to address concerns with rising antimicrobial resistance rates [87-90]. Their successful approaches contrasted with limited activities in Poland to curb rising antibiotic utilisation rates [91]. Limited demand-side measures resulted in Poland continuing having one of the highest rates of antibiotic utilisation rates in Europe between 2007 and 2016 [91].

There are classes of medicines though where health authorities acknowledge it can be difficult to instigate demand-side measures to influence the preferential prescribing of lower cost multiple sourced products. Classes include the atypical antipsychotic medicines for treating schizophrenia and bipolar disease. Concerns with differences in patients' profiles and their needs, as well as the different profiles of the various antipsychotic medicines, have resulted in growing acknowledgment that where possible treatment should be tailored to individual patients [92-95]. We see the same considerations generally for antidepressants [96]. However, demand-side measures have been successfully introduced in Scotland to switch patients from patented escitalopram to multiple sourced citalopram given perceived limited differences in effectiveness alongside considerable cost differences [97]. The combined activities, along with high INN prescribing rates, resulted in a 73.7% reduction in overall expenditure on Selective Serotonin Re-Uptake Inhibitors (SSRIs) between 2001 and 2017 in Scotland despite a 2.34-fold increase in their utilisation [97]. Prescribing restrictions were also successfully introduced for duloxetine in Sweden as the authorities were concerned with its effectiveness and costs versus other multiple-sourced anti-depressants. These restrictions resulted in significantly increased prescribing of multiple sourced venlafaxine, with 3 monthly expenditure on the newer anti-depressants 55% below expenditure prior to the availability of generic venlafaxine soon after the restrictions were introduced [49].

We have also seen similar issues regarding the biosimilars. There have been concerns with their effectiveness and safety

leading to a nocebo affecting challenging their use versus originators [98-100]. However, landmark studies such as the NOR-SWITCH study with biosimilar infliximab in Norway as well as clinical studies demonstrating similar effectiveness and safety with biosimilars, combined with greater knowledge that originator companies can often change their manufacturing process, have enhanced their use [2,22,101-108]. The increasing use of biosimilars is important especially in LMICs where there are issues of access and affordability to biological medicines in the first place [109-111]. In high-income countries, increasing use of biosimilars can offset increasing expenditure on new high-priced medicines for oncology and orphan diseases as well as fund an increasing number of healthcare professionals in clinics to improve patient care where there are concerns [2,112]. Recent studies and reviews have again identified that multiple demand-side measures are necessary to enhance the use of biosimilars; otherwise, their uptake may be limited despite appreciable price reductions [2,9,21,113].

The increased availability of standard medicines for oncology as either lower cost biosimilars or generics should increasingly result in health authorities re-evaluating the prices and/ or discounts for still patented medicines that used these standard medicines for pricing purposes under value-based pricing principles [2,64,114]. We will be monitoring this development given the continued launch of new premium-priced medicines for oncology and orphan diseases and concerns with their impact on continuing to provide comprehensive and universal healthcare for patients with cancer.

In conclusion, we have shown that multiple-sourced medicines are essential to enhance access to standard medicines where co-payments are an issue as well as help fund increased medicine volumes and new premium priced medicines in countries seeking to attain or retain universal healthcare. This also increasingly includes biosimilars. We will continue to monitor ongoing developments to address barriers and concerns with the routine availability of low priced, good quality generics as well as biosimilars to provide direction to others.

REFERENCES

 IQVIA. (2019). The Global Use of Medicine in 2019 and Outlook to 2023 - Forecasts and Areas to Watch.



SCIENTIFIC LITERATURE

- Godman B, Fadare J, Kwon H-Y, Dias CZ, Kurdi A, et al. (2021). Evidence-Based Public Policy Making for Medicines across countries; findings and implications for the future. Journal of Comparative Effectiveness Research. 10: 1019-1052.
- Godman B, Bucsics A, Vella Bonanno P, Oortwijn W, Rothe CC, et al. (2018). Barriers for Access to New Medicines: Searching for the Balance Between Rising Costs and Limited Budgets. Front Public Health. 6: 328.
- Godman B, Wettermark B, van Woerkom M, Fraeyman J, Alvarez-Madrazo S, et al. (2014). Multiple policies to enhance prescribing efficiency for established medicines in Europe with a particular focus on demand-side measures: findings and future implications. Frontiers in pharmacology. 5: 106.
- Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, et al. (2018). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA. 68: 394-424.
- Luzzatto L, Hyry HI, Schieppati A, Costa E, Simoens S, et al. (2018). Outrageous prices of orphan drugs: a call for collaboration. Lancet. 392: 791-794.
- Godman B, Hill A, Simoens S, Selke G, Selke Krulichová I, et al. (2021). Potential approaches for the pricing of cancer medicines across Europe to enhance the sustainability of healthcare systems and the implications. Expert review of pharmacoeconomics & outcomes research. 11: 1-14.
- Morgan SG, Bathula HS, Moon S. (2020). Pricing of pharmaceuticals is becoming a major challenge for health systems. BMJ. 368: 14627.
- Godman B, Haque M, Leong T, Allocati E, Kumar S, et al. (2021). The Current Situation Regarding Long-Acting Insulin Analogues Including Biosimilars Among African, Asian, European, and South American Countries; Findings and Implications for the Future. Frontiers in Public Health. 9.
- Moon S, Mariat S, Kamae I, Pedersen HB. (2020). Defining the concept of fair pricing for medicines. BMJ. 368: 14726.
- 11. Suleman F, Low M, Moon S, Morgan SG. (2020). New business models for research and development with

affordability requirements are needed to achieve fair pricing of medicines. BMJ. 368: 14408.

- Cameron A, Ewen M, Ross-Degnan D, Ball D, Laing R. (2009). Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis. Lancet. 373: 240-249.
- Ofori-Asenso R, Agyeman AA. (2016). Irrational Use of Medicines—A Summary of Key Concepts. Pharmacy 4: 35.
- Fadare J, Olamoyegun M, Gbadegesin BA. (2015). Medication adherence and direct treatment cost among diabetes patients attending a tertiary healthcare facility in Ogbomosho, Nigeria. Malawi Med J. 27: 65-70.
- Mutyambizi C, Pavlova M, Chola L, Hongoro C, Groot W. (2018). Cost of diabetes mellitus in Africa: a systematic review of existing literature. Global Health. 14: 3.
- 16. Kastor A, Mohanty SK. (2018). Disease-specific out-ofpocket and catastrophic health expenditure on hospitalization in India: Do Indian households face distress health financing? PIoS one. 13: e0196106.
- Rahman MM, Zhang C, Swe KT, Rahman MS, Islam MR, et al. (2020). Disease-specific out-of-pocket healthcare expenditure in urban Bangladesh: A Bayesian analysis. PloS one. 15: e0227565.
- Aregbeshola BS, Khan SM. (2018). Out-of-Pocket Payments, Catastrophic Health Expenditure and Poverty Among Households in Nigeria 2010. International journal of health policy and management. 7: 798-806.
- Hogan DR, Stevens GA, Hosseinpoor AR, Boerma T. (2018). Monitoring universal health coverage within the Sustainable Development Goals: development and baseline data for an index of essential health services. The Lancet Global health. 6: e152-e68.
- Gyasi RM, Phillips DR. (2020). Aging and the Rising Burden of Noncommunicable Diseases in Sub-Saharan Africa and other Low- and Middle-Income Countries: A Call for Holistic Action. The Gerontologist. 60: 806-811.
- Godman B, Allocati E, Moorkens E, Kwon H-Y. (2020). Can local policies on biosimilars optimize the use of freed resources – experiences from Italy. Generics and Biosimilars Initiative Journal (GABI). 9: 183-187.





- Moorkens E, Vulto AG, Huys I, Dylst P, Godman B, et al. (2017). Policies for biosimilar uptake in Europe: An overview. PloS one. 12: e0190147.
- Godman B. (2021). Biosimilars are becoming indispensable in the management of multiple diseases although concerns still exist. Bangladesh Journal of Medical Science. 20: 5-10.
- Cameron A, Mantel-Teeuwisse AK, Leufkens HG, Laing RO. (2012). Switching from originator brand medicines to generic equivalents in selected developing countries: how much could be saved? Value in health. 15: 664-673.
- 25. Moe-Byrne T, Chambers D, Harden M, McDaid C. (2014). Behaviour change interventions to promote prescribing of generic drugs: a rapid evidence synthesis and systematic review. BMJ open. 4: e004623.
- 26. Corrao G, Soranna D, Merlino L, Mancia G. (2014). Similarity between generic and brand-name antihypertensive drugs for primary prevention of cardiovascular disease: evidence from a large populationbased study. European journal of clinical investigation. 44: 933-939.
- 27. Corrao G, Soranna D, La Vecchia C, Catapano A, Agabiti-Rosei E, et al. (2014). Medication persistence and the use of generic and brand-name blood pressure-lowering agents. Journal of hypertension. 32: 1146-1153.
- Manzoli L, Flacco ME, Boccia S, D'Andrea E, Panic N, et al. (2016). Generic versus brand-name drugs used in cardiovascular diseases. European journal of epidemiology. 31: 351-368.
- Corrao G, Soranna D, Arfe A, Casula M, Tragni E, et al. (2014). Are generic and brand-name statins clinically equivalent? Evidence from a real data-base. European journal of internal medicine. 25: 745-750.
- Kesselheim AS, Misono AS, Lee JL, Stedman MR, Brookhart MA, et al. (2008). Clinical equivalence of generic and brand-name drugs used in cardiovascular disease: a systematic review and meta-analysis. Jama. 300: 2514-2526.
- Paton C. (2006). Generic clozapine: outcomes after switching formulations. The British journal of psychiatry. 189: 184-185.

- 32. Lin YS, Jan IS, Cheng SH. (2017). Comparative analysis of the cost and effectiveness of generic and brand-name antibiotics: the case of uncomplicated urinary tract infection. Pharmacoepidemiol Drug Saf. 26: 301-309.
- Fadare JO, Adeoti AO, Desalu OO, Enwere OO, Makusidi AM, et al. (2016). The prescribing of generic medicines in Nigeria: knowledge, perceptions and attitudes of physicians. Expert review of pharmacoeconomics & outcomes research. 16: 639-650.
- 34. Khan B, Godman B, Babar A, Hussain S, Mahmood S, et al. (2016). Assessment of active pharmaceutical ingredients in drug registration procedures in Pakistan: implications for the future. Generics and Biosimilars Initiative Journal (GaBI Journal). 5: 156-163.
- 35. GABI online. (2012). Poor quality pharma ingredients abound in China.
- GABI Online. (2016). China introduces new quality and efficacy requirements for generics.
- Management Sciences for Health. (2018). Building a Resilient Pharmaceutical System: SIAPS Event Highlights its Work in Namibia.
- Sermet C, Andrieu V, Godman B, Van Ganse E, Haycox A, et al. (2010). Ongoing pharmaceutical reforms in France: implications for key stakeholder groups. Applied health economics and health policy. 8: 7-24.
- Garuoliene K, Godman B, Gulbinovic J, Wettermark B, Haycox A. (2011). European countries with small populations can obtain low prices for drugs: Lithuania as a case history. Expert review of pharmacoeconomics & outcomes research. 11: 343-349.
- 40. Godman B, Wettermark B, Hoffmann M, Andersson K, Haycox A, et al. (2009). Multifaceted national and regional drug reforms and initiatives in ambulatory care in Sweden: global relevance. Expert review of pharmacoeconomics & outcomes research. 9: 65-83.
- Duerden MG, Hughes DA. (2010). Generic and therapeutic substitutions in the UK: are they a good thing? British journal of clinical pharmacology. 70: 335-341.
- 42. Ferner RE, Lenney W, Marriott JF. (2010). Controversy over generic substitution. BMJ. 340: c2548.
- 43. MHRA. (2017). Antiepileptic drugs: updated advice on switching between different manufacturers' products.







- 44. Godman B, Baumgartel C. (2015). Are generic immunosuppressants safe and effective? BMJ. 350: h3248.
- 45. Godman B, Bishop I, Finlayson AE, Campbell S, Kwon HY, et al. (2013). Reforms and initiatives in Scotland in recent years to encourage the prescribing of generic drugs, their influence and implications for other countries. Expert review of pharmacoeconomics & outcomes research. 13: 469-482.
- 46. Leporowski A, Godman B, Kurdi A, MacBride-Stewart S, Ryan M, et al. (2018). Ongoing activities to optimize the quality and efficiency of lipid-lowering agents in the Scottish national health service: influence and implications. Expert review of pharmacoeconomics & outcomes research. 18: 655-666.
- 47. McGinn D, Godman B, Lonsdale J, Way R, Wettermark B, et al. (2010). Initiatives to enhance the quality and efficiency of statin and PPI prescribing in the UK: impact and implications. Expert review of pharmacoeconomics & outcomes research. 10: 73-85.
- Andersson K, Jörgensen T, Carlsten A. (2006). Physicians' opinions and experiences of the Pharmaceutical Benefits Reform. Scandinavian journal of public health. 34: 654-659.
- 49. Godman B, Persson M, Miranda J, Skiold P, Wettermark B, et al. (2013). Changes in the utilization of venlafaxine after the introduction of generics in Sweden. Applied health economics and health policy. 11: 383-393.
- 50. Godman B, Wettermark B, Miranda J, Bennie M, Martin A, et al. (2013). Influence of multiple initiatives in Sweden to enhance ARB prescribing efficiency following generic losartan; findings and implications for other countries. International journal of clinical practice. 67: 853-862.
- 51. Olsson E, Wallach-Kildemoes H, Ahmed B, Ingman P, Kaae S, et al. (2017). The influence of generic substitution on the content of patient-pharmacist communication in Swedish community pharmacies. The International journal of pharmacy practice. 25: 274-281.
- 52. Martin A, Godman B, Miranda J, Tilstone J, Saleem N, et al. (2014). Measures to improve angiotensin receptor blocker prescribing efficiency in the UK: findings and implications. Journal of comparative effectiveness research. 3: 41-51.

- 53. Olsson E, Kälvemark Sporrong S. (2012). Pharmacists' experiences and attitudes regarding generic drugs and generic substitution: two sides of the coin. The International journal of pharmacy practice. 20: 377-383.
- 54. Arnet I, Altermatt M, Roggo Y, Schnetzler G. (2014). Pharmaceutical quality of eight generics of ceftriaxone preparation for injection in Eastern Asia. Journal of chemotherapy. 27: 337-342.
- 55. Redfern J, Kaur H, Adedoyin RA, Ofori S, Anchala R, et al. (2019). Equivalence in Active Pharmaceutical Ingredient of Generic Antihypertensive Medicines Available in Nigeria (EQUIMEDS): A Case for Further Surveillance. Global heart. 14: 327-333.
- 56. Coyne PE. (2019). The World Health Organization Prequalification Programme-playing an essential role in assuring quality medical products. Int Health. 11: 79-80.
- 57. Newton PN, Hanson K, Goodman C. (2017). Do antimalarials in Africa meet quality standards? The market penetration of non quality-assured artemisinin combination therapy in eight African countries. Malar J. 16: 204.
- 58. WHO. (2020). Launch of the Lomé Initiative.
- 59. Gwaza L, Gordon J, Welink J, Potthast H, Leufkens H, Stahl M, et al. (2014). Adjusted indirect treatment comparison of the bioavailability of WHO-prequalified first-line generic antituberculosis medicines. Clinical pharmacology and therapeutics. 96: 580-588.
- Editorial. (2016). Generic medicines Interchangeability of WHO-prequalified generics. WHO Drug Information. 30: 370-375.
- Baumgärtel C, Godman B, Malmström R, Andersen M, Abuelkhair M, et al. (2012). What lessons can be learned from the launch of generic clopidogrel? GaBI Journal. 1: 58-68.
- 62. Editorial. (2013). Generic bashing: effective but illegal. Rev Prescrire. 33: 773.
- 63. Godman B, Wilcock M, Martin A, Bryson S, Baumgärtel C, et al. (2015). Generic pregabalin; current situation and implications for health authorities, generics and biosimilars manufacturers in the future. GaBI Journal. 4: 125-135.
- 64. Godman B, Hill A, Simoens S, Kurdi A, Gulbinovič J, et al. (2019). Pricing of oral generic cancer medicines in 25



SCIENTIFIC LITERATURE

European countries; findings and implications. Generics and Biosimilars Initiative Journal (GaBI Journal). 8: 49-70.

- 65. Woerkom M, Piepenbrink H, Godman B, Metz J, Campbell S, et al. (2012). Ongoing measures to enhance the efficiency of prescribing of proton pump inhibitors and statins in The Netherlands: influence and future implications. Journal of comparative effectiveness research. 1: 527-538.
- 66. Godman B, Abuelkhair M, Vitry A, Abdu S, Bennie M, et al. (2012). Payers endorse generics to enhance prescribing efficiency: impact and future implications, a case history approach. 1: 69-83.
- 67. Yu SY, Yang BM, Kim JH. (2013). New anti-rebate legislation in South Korea. Applied health economics and health policy. 11: 311-318.
- 68. Dylst P, Vulto A, Godman B, Simoens S. (2013). Generic medicines: solutions for a sustainable drug market? Applied health economics and health policy. 11: 437-443.
- Acosta A, Vanegas EP, Rovira J, Godman B, Bochenek T. (2019). Medicine Shortages: Gaps Between Countries and Global Perspectives. Frontiers in pharmacology. 10: 763.
- 70. McKee M, Stuckler D, Martin-Moreno JM. (2010). Protecting health in hard times. BMJ. 341: c5308.
- 71. Abuelkhair M, Abdu S, Godman B, Fahmy S, Malmstrom RE, et al. (2012). Imperative to consider multiple initiatives to maximize prescribing efficiency from generic availability: case history from Abu Dhabi. Expert review of pharmacoeconomics & outcomes research. 12: 115-124.
- 72. Kwon HY, Kim H, Godman B, Reich MR. (2015). The impact of South Korea's new drug-pricing policy on market competition among off-patent drugs. Expert review of pharmacoeconomics & outcomes research. 15: 1007-1014.
- Kwon HY, Godman B. (2017). Drug Pricing in South Korea. Applied health economics and health policy. 15: 447-453.
- 74. Godman B, Shrank W, Wettermark B, Andersen M, Bishop I, et al. (2010). Use of Generics-A Critical Cost Containment Measure for All Healthcare Professionals in Europe? Pharmaceuticals. 3: 2470-2494.
- 75. Godman B, Shrank W, Andersen M, Berg C, Bishop I, et al. (2010). Comparing policies to enhance prescribing efficiency in Europe through increasing generic utilization:

changes seen and global implications. Expert review of pharmacoeconomics & outcomes research. 10: 707-722.

- 76. Godman B, Shrank W, Andersen M, Berg C, Bishop I, et al. (2010). Policies to enhance prescribing efficiency in europe: findings and future implications. Frontiers in pharmacology. 1: 141.
- 77. Heart Protection Study Collaborative Group. (2002). MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. Lancet. 360: 7-22.
- Strandberg TE, Pyorala K, Cook TJ, Wilhelmsen L, Faergeman O, et al. (2004). Mortality and incidence of cancer during 10-year follow-up of the Scandinavian Simvastatin Survival Study (4S). Lancet. 364: 771-777.
- 79. Godman B, Kurdi A, McCabe H, MacBride-Stewart S, Leporowski A, et al. (2018). Ongoing activities to influence the prescribing of proton pump inhibitors within the Scottish National Health Service: their effect and implications. Generics and Biosimilars Initiative Journal (GaBI Journal). 7: 142-151.
- Voncina L, Strizrep T, Godman B, Bennie M, Bishop I, et al. (2011). Influence of demand-side measures to enhance renin-angiotensin prescribing efficiency in Europe: implications for the future. Expert review of pharmacoeconomics & outcomes research. 11: 469-479.
- Moon JC, Godman B, Petzold M, Alvarez-Madrazo S, Bennett K, et al. (2014). Different initiatives across Europe to enhance losartan utilization post generics: impact and implications. Frontiers in pharmacology. 5: 219.
- Hesse U, Godman B, Petzold M, Martin A, Malmstrom RE. (2013). Impact of delisting ARBs, apart from losartan, on ARB utilisation patterns in Denmark: implications for other countries. Applied health economics and health policy. 11: 677-685.
- Bucsics A, Godman B, Burkhardt T, Schmitzer M, Malmstrom RE. (2012). Influence of lifting prescribing restrictions for losartan on subsequent sartan utilization patterns in Austria: implications for other countries. Expert review of pharmacoeconomics & outcomes research. 12: 809-819.
- Simoens S, De Bruyn K, Miranda J, Bennie M, Malmström RE, et al. (2013). Measures to enhance angiotensinreceptor blocker prescribing efficiency in Belgium

Generic Drugs – Essential for the Sustainability of Healthcare Systems with Numerous Strategies to Enhance their Use. Pharmaceutical Sciences And Biomedical Analysis Journal. 2022; 4(1):126.

following generic losartan: impact and implications for the future. Journal of Pharmaceutical Health Services Research. 4: 173-181.

- 85. Bennie M, Bishop I, Godman B, Campbell S, Miranda J, et al. (2013). Are prescribing initiatives readily transferable across classes: the case of generic losartan in Scotland? Quality in primary care. 21: 7-15.
- 86. Kurdi A, Elliott RA, Chen L-C. (2020). Lessons from the failure of implementing the 'Better Care Better Value' prescribing indicator for renin–angiotensin system drugs in England: a qualitative study of general practitioners' perceptions using behavioural change framework. BMJ open. 10: e035910.
- Abilova V, Kurdi A, Godman B. (2018). Ongoing initiatives in Azerbaijan to improve the use of antibiotics; findings and implications. Expert review of anti-infective therapy. 16: 77-84.
- 88. Furst J, Cizman M, Mrak J, Kos D, Campbell S, et al. (2015). The influence of a sustained multifaceted approach to improve antibiotic prescribing in Slovenia during the past decade: findings and implications. Expert review of anti-infective therapy. 13: 279-289.
- 89. Bojanic L, Markovic-Pekovic V, Skrbic R, Stojakovic N, Ethermanovic M, et al. (2018). Recent Initiatives in the Republic of Srpska to Enhance Appropriate Use of Antibiotics in Ambulatory Care; Their Influence and Implications. Frontiers in pharmacology. 9: 442.
- 90. Godman B, Haque M, McKimm J, Abu Bakar M, Sneddon J, et al. (2020). Ongoing strategies to improve the management of upper respiratory tract infections and reduce inappropriate antibiotic use particularly among lower and middle-income countries: findings and implications for the future. Current medical research and opinion. 36: 301-327.
- Wojkowska-Mach J, Godman B, Glassman A, Kurdi A, Pilc A, et al. (2018). Antibiotic consumption and antimicrobial resistance in Poland; findings and implications. Antimicrobial Resistance & Infection Control. 7: 136.
- Parks J, Radke A, Parker G, Foti ME, Eilers R, et al. (2009).
 Principles of antipsychotic prescribing for policy makers, circa 2008. Translating knowledge to promote

individualized treatment. Schizophrenia bulletin. 35: 931-936.

- P3. Leucht S, Cipriani A, Spineli L, Mavridis D, Orey D, et al. (2013). Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis. Lancet. 382: 951-962.
- 94. Godman B, Petzold M, Bennett K, Bennie M, Bucsics A, et al. (2014). Can authorities appreciably enhance the prescribing of oral generic risperidone to conserve resources?: Findings from across Europe and their implications. BMC medicine. 12: 98.
- 95. Godman B. (2015). The need for cost-effective choices to treat patients with bipolar 1 disorders including asenapine. Journal of medical economics. 18: 871-873.
- 96. Godman B, Bucsics A, Burkhardt T, Piessnegger J, Schmitzer M, et al. (2013). Potential to enhance the prescribing of generic drugs in patients with mental health problems in austria; implications for the future. Frontiers in pharmacology. 3: 198.
- 97. Godman B, Kurdi A, McCabe H, Johnson CF, Barbui C, et al. (2019). Ongoing initiatives within the Scottish National Health Service to affect the prescribing of selective serotonin reuptake inhibitors and their influence. Journal of comparative effectiveness research. 8: 535-547.
- Class JN, Langis L. (2012). A patient-centred paradigm for the biosimilars market. Generics and Biosimilars Initiative Journal (GaBI Journal). 1: 17-21.
- Lee JF, Litten JB, Grampp G. (2012). Comparability and biosimilarity: considerations for the healthcare provider. Current medical research and opinion. 28: 1053-1058.
- Colloca L, Panaccione R, Murphy TK. (2019). The Clinical Implications of Nocebo Effects for Biosimilar Therapy. Frontiers in pharmacology. 10.
- 101. Jorgensen KK, Olsen IC, Goll GL, Lorentzen M, Bolstad N, et al. (2017). Switching from originator infliximab to biosimilar CT-P13 compared with maintained treatment with originator infliximab (NOR-SWITCH): a 52-week, randomised, double-blind, non-inferiority trial. Lancet. 389: 2304-2316.
- 102. Høivik ML, Buer LCT, Cvancarova M, Warren DJ, Bolstad N, et al. (2018). Switching from originator to biosimilar infliximab - real world data of a prospective 18

Generic Drugs – Essential for the Sustainability of Healthcare Systems with Numerous Strategies to Enhance their Use. Pharmaceutical Sciences And Biomedical Analysis Journal. 2022; 4(1):126.



SCIENTIFIC LITERATURE

months follow-up of a single-centre IBD population. Scandinavian journal of gastroenterology. 53: 692-699.

- 103. Pegram MD, Bondarenko I, Zorzetto MMC, Hingmire S, Iwase H, et al. (2019). PF-05280014 (a trastuzumab biosimilar) plus paclitaxel compared with reference trastuzumab plus paclitaxel for HER2-positive metastatic breast cancer: a randomised, double-blind study. Br J Cancer. 120: 172-182.
- 104. Barbier L, Ebbers HC, Declerck P, Simoens S, Vulto AG, et al. (2020). The Efficacy, Safety, and Immunogenicity of Switching Between Reference Biopharmaceuticals and Biosimilars: A Systematic Review. Clinical pharmacology and therapeutics. 108: 734-755.
- 105. Moorkens E, Godman B, Huys I, Hoxha I, Malaj A, et al. (2021). The expiry of Humira ® market exclusivity and the entry of adalimumab biosimilars in Europe: An overview of pricing and national policy measures. Frontiers in pharmacology. 11: 591134.
- 106. Stebbing J, Baranau YV, Baryash V, Manikhas A, Moiseyenko V, et al. (2017). Double-blind, randomized phase III study to compare the efficacy and safety of CT-P6, trastuzumab biosimilar candidate versus trastuzumab as neoadjuvant treatment in HER2 positive early breast cancer (EBC). Journal of Clinical Oncology. 35: 510.
- 107. Jimenez-Pichardo L, Gazquez-Perez R, Sierra-Sanchez JF. (2018). Degree of prescriber's knowledge about variability in biological drugs "innovators" in manufacturing process. European journal of clinical pharmacology. 74: 505-511.
- 108. Vezer B, Buzas Z, Sebeszta M, Zrubka Z. (2016). Authorized manufacturing changes for therapeutic monoclonal antibodies (mAbs) in European Public Assessment Report (EPAR) documents. Current medical research and opinion. 32: 829-834.

- 109. Gershon N, Berchenko Y, Hall PS, Goldstein DA. (2019). Cost effectiveness and affordability of trastuzumab in sub-Saharan Africa for early stage HER2positive breast cancer. Cost effectiveness and resource allocation: 17: 5.
- Baumgart DC, Misery L, Naeyaert S, Taylor PC.
 Biological Therapies in Immune-Mediated Inflammatory Diseases: Can Biosimilars Reduce Access Inequities? Frontiers in pharmacology. 10: 279.
- 111. Kostic M, Djakovic L, Sujic R, Godman B, Jankovic SM. (2017). Inflammatory Bowel Diseases (Crohn s Disease and Ulcerative Colitis): Cost of Treatment in Serbia and the Implications. Applied health economics and health policy. 15: 85-93.
- 112. Dutta B, Huys I, Vulto AG, Simoens S. (2020). Identifying Key Benefits in European Off-Patent Biologics and Biosimilar Markets: It is Not Only About Price! BioDrugs. 34: 159-170.
- 113. Kim Y, Kwon H-Y, Godman B, Moorkens E, Simoens S, et al. (2020). Uptake of Biosimilar Infliximab in the UK, France, Japan, and Korea: Budget Savings or Market Expansion Across Countries? Frontiers in pharmacology. 11.
- 114. Godman B, Hill A, Simoens S, Selke G, Selke Krulichová I, et al. (2021). Potential approaches for the pricing of cancer medicines across Europe to enhance the sustainability of healthcare systems and the implications. Expert review of pharmacoeconomics & outcomes research. 1-14.



011