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Short communication

# Is there a need for a formulary of clinically interchangeable medicines to guide generic substitution in Saudi Arabia?

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ABSTRACT

The escalating healthcare expenditure is a major challenge to sustainability of the healthcare systems. To confront the escalating health expenditure in general and medicines expenditure in particular, many countries promoted the use of generic medicines. To promote generic medicines, many countries have adopted a generic substitution (GS) policy and generic prescribing. To effectively implement the GS policy, it is evident in the literature that it is essential to have an evidence-based guide on therapeutic equivalence and formulary of interchangeable medicines to guide responsible GS. In Saudi Arabia, GS is permissive and pharmacists are given the right to perform GS. While the prescriber's approval is not a requirement, patient consent is required when performing GS. Although there are some general drug references, such as the Saudi National Formulary (SNF) and list of registered medicines in the Saudi market, but there is currently no information available to healthcare professionals that documents the therapeutic and bioequivalence between medicines. Thus, it is essential to have a formulary of interchangeable medicines to guide appropriate GS or at least to include such vital information regarding therapeutic equivalence and brand interchangeability as part of the SNF. That, in turn, will not only make healthcare professionals more confident when providing GS, but will also enable the avoidance of situations where GS is inappropriate.



## 1. The role of generic medicines in sustainability of healthcare systems

To confront the escalating health expenditure in general and medicine expenditure in particular, the use of generic medicines is promoted and encouraged in many countries.[1,2] Indeed, generic medicine utilization has led to substantial cost savings for the healthcare system.[3–7] While generic medicines lead to substantial cost savings to the healthcare system, they provide the same health outcomes.[8] In fact, generic medicines, as equivalent versions of original brand medicines, are considered cost effective first line and standard therapy for many diseases and conditions such as hypertension, diabetes, asthma, allergies, depression, gastrointestinal disorders, infections, skin diseases, HIV/AIDS and many other diseases and conditions.[6,9] Thus, by using generic medicines, the healthcare system can save a huge amount of money that can be utilized to pay for the more expensive patented and new innovative products that are needed to treat some diseases where generic medicines are not available.[10] Hence, the wide use of generic medicines is instrumental to the creation and maintenance of sustainable healthcare systems.[11] Therefore, healthcare professionals are encouraged to promote generic medicines to their patients.

## 2. Generic substitution as a method to promote generic medicines

To promote generic medicines, generic substitution (GS) and generic prescribing are adopted in many healthcare systems.[12] GS can be defined as an act of dispensing an equivalent generic medicine when a branded medicine is prescribed (i.e. switching the patient from an original brand medicine to an equivalent generic medicine), while generic prescribing is defined as prescribing by the approved Non-Proprietary Name (INN) of the medicines.[13] However, GS is not a simple task that involves switching from an original brand to another, but rather a task that should be done after considering

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many factors related to the medicine itself, the patient, the physicians and the regulations, and should be based on several clinical and non-clinical considerations. The considerations include patient preference, patient consent, prescriber's approval (if needed), patient's understanding of the difference between the medicine brands to prevent any confusion due to brand changing (especially for some patients, e.g. the elderly), consistency in the selection of the brand especially for chronic and long-term therapy, the assessment of allergy history to any inactive ingredients, if the new brand needs different instructions to handle, and the patient's familiarity with the brand (e.g. metered dose dry powder inhalers, somatropin injection cartridges).[14–18] In addition, patients need to be educated about generic medicines in terms of quality, safety, efficacy, bioequivalence and the similarities and differences between them and the original brands. Therefore, healthcare professionals need to assess the suitability of GS based on their professional judgment.[19] However, more importantly, one of the essential steps in performing GS is that the generic medicine must be bioequivalent and therapeutically equivalent to the original brand medicine. Thus, unlike other factors that need to be considered when performing GS, therapeutic equivalence should be based on scientific evidence rather than professional judgment of individual healthcare professionals, as GS is not appropriate for some medicines. For example, Narrow Therapeutic Index (NTI) drugs such as anti-arrhythmic drugs (e.g. Digoxin, disopyramide), anticoagulant drugs (e.g. Warfarin), antiepileptic drugs (e.g. Carbamazepine, phenytoin, valproic acid), and anti-rejection drugs (e.g. Cyclosporine, sirolimus, tacrolimus). Other examples include modified release preparations of medicines (e.g. carbamazepine, theophylline, diltiazem, aminophylline, nifedipine, morphine and oxycodone), medicines containing more than one active ingredient (e.g. some topical preparations, oral contraceptives, antacids preparations containing simethicone), different products of the same active ingredient that have different licensed indications (e.g. sildenafil (Viagra® or Revatio®)), and products using different salts to form the active ingredients (e.g. amitriptyline, nortriptyline).[13,18,20,21]

Therefore, many countries have produced evidence-based guides to ensure that GS is appropriate. One of the examples is the "Approved Drug Products with Therapeutic Equivalence Evaluations", commonly known as the Orange Book,[19] which is a useful guide for pharmacists and other healthcare professionals as regards therapeutic equivalence and approved generic medicines in the US. In this list, products that are therapeutically equivalent where there is adequate evidence supporting bioequivalence are designated with a code "A", and products that are not therapeutically equivalent, where there is no adequate evidence supporting bioequivalence, are designated with a code "B". Another example is the Schedule of Pharmaceutical benefits in Australia, which is a useful guide for healthcare professionals and consumers as regards therapeutic equivalence between medicines.[22] In the Australian schedule, "a" precedes the names of therapeutically equivalent and interchangeable medicine brands, whereas "b" is attached to brands of the medicine that are equivalent to the original brand but there is no evidence of equivalency between them and other products marked with "a". For other medicines not marked with a or b, their therapeutic equivalence is not known; hence, caution should be exercised when GS is done. In Denmark, The Royal Dutch Pharmacists Association (KNMP) has produced a professional guideline for community pharmacists regarding GS. The guideline is aimed to help CPs to perform GS appropriately by providing principles and guidance when performing GS. The guideline addressed the issue of NTI drugs and other drugs for which GS is not appropriate. In addition, it addressed the prescription of biological and biosimilars. Furthermore, it addressed random substitution and the general considerations and factors that need to be taken into account, such as the factors related to patients, factors related to prescribers and legal issues.[23,24]

## 3. Generic substitution in Saudi Arabia

In Saudi Arabia, generic medicines are registered via an evidence-based rigorous scientific process to ensure the efficacy, safety and quality of medicines.[25] Furthermore, Saudi Food and Drug Authority (SFDA), which is the drug regulatory body in Saudi Arabia, requires the demonstration of bioequivalence before registration and it can be waived only if scientifically appropriate.[26] Registered medicines are listed in the Saudi National Formulary (SNF) and are also listed in the directory of registered medicines in Saudi Arabia, which can be accessed online via the SFDA website.[27] The SNF contains full prescribing information about registered medicines, including trade names of products and their prices. However, there is no information in the SNF about bioequivalence evaluation and therapeutic interchangeability to guide GS and generic prescribing by healthcare professionals.

In Saudi Arabia, GS is permissive, as pharmacists are allowed to perform generic substitution according to article no. 23 of the Practice of Health Professions Act 2005. While prescriber's permission is not a requirement, patient consent is required.[28] Pharmacists are not allowed to perform generic substitution for Narrow Therapeutic Index (NTI) Drugs according the Executive Regulations of Practice of Health Profession Act 2006.[29] However, there is no list available to pharmacists and other healthcare professionals about NTI drugs and other medicines that are not suitable for GS.

To guide GS, there is evidence in the literature of the importance of having a formulary of interchangeable medicines to facilitate appropriate GS.[30–33] For instance, Johnston et al (2011) recommended that evidence regarding therapeutic equivalence should be made available to the public and that best practice guidelines are required for GS.[33] Furthermore, Hassali et al (2012) concluded that to promote responsible generic substitution, a formulary of interchangeable medicines must be developed to guide GS. The formulary should also contain the list of the products that are not suitable for GS; such a formulary would help both prescribers and pharmacists to assess the generic equivalence of the products offered as alternative substitutes.[32]

## 4. Conclusion

In conclusion, we believe that it is instrumental to have a formulary of interchangeable products to guide responsible GS or at least include such vital information in the SNF to make healthcare professionals more confident when providing GS and to avoid situations where GS is inappropriate.

## Conflicts of interest

All authors have none to declare.

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