EDITORIAL

ARE GENERICS EQUIVALENT TO ORIGINATOR BRANDS?

The term 'generic medicine' often elicits a negative connotation about the drug product in question as being a copy, imitation, substandard, counterfeit, fake or cheap poor alternative. Other perceptions by lay people and healthcare professionals, denote diminished quality, safety and efficacy. Generic drugs are designed to have the same active ingredient, dosage form, route of administration, strength, safety, efficacy and indications as the innovator brands. The World Health Organization (WHO) specification further requires that generics be bioequivalent to originator medicines.

Generics drug products are substantially cheaper compared to the innovator brands due to dispensation from incurment of drug development costs. Instead, the developers of the generic product need to demonstrate therapeutic equivalence through pharmaceutical- and bio-equivalence data. Therapeutic equivalence confers interchangeability with originator brands in routine clinical applications due to similarity in quality and performance characteristics. Some developing countries, however, lack capacity to perform bioequivalence studies locally, thus leading to use alternative evaluations. In Kenya, imported generic products are evaluated based on data obtained in the countries of origin while local manufacturers provide comparative dissolution reports as surrogate for bioequivalence.

Several published reports have demonstrated that generic formulations have quality problems especially when analysed for identity, assay and dissolution tests (for tablets and capsules). Such literature resources, as well as personal experiences and perceptions have driven prescribers to prefer innovator brands. The resultant professional behaviors have caused a barrier to wide acceptance of generics in healthcare systems. This undermines generic prescribing and dispensing which are the hallmarks of cost saving for insurers and healthcare payers. In addition, government (public) facilities heavily depend on generics for their drug needs due to affordability. However, the proviso for generics use, is that registered products in the market are comprehensively evaluated by the drug regulatory authorities for therapeutic equivalence.

Pharmaceutical equivalence requires a deeper investigation of product properties that cannot be easily elucidated through routine analysis i.e. identity, assay and single point dissolution. The constituent excipients and product design differ between the innovator and generics, which in turn affects drug release and absorption hence the need to demonstrate similarity between the two. Therefore, a comparative dissolution at three pH levels (1.2, 4.5 and 6.8) against the originator product is carried out. The International Conference on Harmonization (ICH) has provided the fit factors, f1 (difference factor) and f2 (similarity factor) for comparative dissolution of generic with originator products. The acceptance criteria for f1 and f2 are less than 10 and more than 50 respectively. Generic products that do not meet these specifications are not pharmaceutically equivalent and by extension not interchangeable.

An article in this issue of the journal by Minyetto et al. demonstrates that routine quality tests will not reveal intrinsic product properties, based on product design that impact on efficacy and safety. Despite, the samples complying with specifications for identity, weight uniformity, disintegration and assay, about 50% of the ciprofloxacin generics studied were not equivalent to the originator brand, Cipro® according to comparative dissolution results. Similarly, a previous study by Manani et al. (Sci. Pharm. 85, 20) on clarithromycin recorded a 75% non-compliance rate upon comparative dissolution. This is a worrying trend given that comparative dissolution is a surrogate for bioavailability. Independently, market surveillance and pharmacovigilance studies have encountered substandard generic products.

These findings should serve as a wakeup call for the Pharmacy and Poisons Board (PPB), to work towards the establishment of a bioequivalence centre in Kenya, in conformity with international best practices. The centre will be instrumental in regulatory evaluation of pharmaceutical products and ensure availability of quality assured generics in the market. Establishment of the centre will of course attract heavy investment in buildings, laboratory infrastructure, equipment and specialized man power to support operations. Thus, financial investment from the government and enabling legal provisions are required. This also calls for

collaboration of the regulator (PPB), academia and the pharmaceutical industry to exploit the unique resources held by these players. The prospect of such a bioequivalence centre evolving into a regional hub should give impetus to this cause.

In addition, regular market surveillance should be instituted by the PPB, to curb circulation of substandard and falsified products. It goes without saying that generics are the mainstay of drug needs in the patient management process. Concerted efforts from manufacturers, regulators, and supply chain players are crucial in ensuring that quality-assured generics are available in the market. Overall, these strategies will inspire confidence among prescribers and users towards generics thus reducing the cost of healthcare and improving availability of affordable drugs in the market.

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