

## More Vigilance on Generic Drugs are Necessary

Sir,

Vildagliptin and its combination with metformin are among the most commonly used antidiabetic drugs in India. With the expiry of patent, there is an explosion of generic Vildagliptin in India. Generic drugs being cheaper will result in a significant reduction in costs and better adherence. However, prescribers should be aware of the differences from the branded drug and the difference among various generics.

Generic drugs should be identical or within an acceptable bioequivalent range to the branded drug with respect to pharmacokinetic and pharmacodynamics properties. Central Drugs Standard Control Organization (CDSCO) requires bioavailability (BA)/bioequivalence (BE) studies to be conducted on the generic drug prior to approval.<sup>[1]</sup> These single-dose studies are done in healthy individuals with normal BMI, 18–60 years of age and with normal renal functions. As per CDSCO, the confidence interval for the ratio of geometric means of area under the plasma concentration curve (AUC) and maximum plasma concentration (C<sub>max</sub>) determined using log-transformed data should generally be within the range of 80% to 125%, when the generic is compared to the reference (brand) product after single-dose administration. The procedures leading to approval of the drug are stringent, with emphasis on the BA/BE studies from approved labs, analytical procedures, excipients, manufacturing process, impurities characterization, etc. However, most branded molecules world over are first submitted to regulatory agencies like USFDA or EMA. The results of PK/PD studies, the toxicity studies, phase I-III clinical trials, and studies in special populations like elderly and in renal and hepatic dysfunction are available in public domain.<sup>[2]</sup> However, BA/BE studies of generics in India are not usually available in the public domain to be scrutinized by the practicing physician.

Concerns have been raised that generic drugs may not be identical to that of originator molecules.<sup>[3]</sup> This could be due to reasons that are beyond the testing capabilities of BA/BE studies. All drug products are formulated with Active Pharmaceutical Ingredients (API) and excipients. The major cost of the drug is the cost of API. API of the branded drug may differ from generic in terms of various synthesis related (e.g., starting material, impurities, residual solvents, polymorphism, isomerism, and manufacturing process) and formulation related factors (solubility, particle size, bulk density, polymorphism, and flowability).<sup>[4]</sup> Changes in the API supplier subsequently over the years may affect the quality of the drug.

Excipients are ingredients other than the API that comprise a completed dosage form. It acts as a carrier and contributes to the stability, appearance, and biopharmaceutical profile of the drug. Generics may have excipients which can differ from the brand drugs and may affect the drug concentration in steady state.<sup>[5]</sup> It is well known that various forms of branded and generic levothyroxine preparations if interchanged may lead to a difference in therapeutic efficacy. Further, in fixed drug combinations (e.g., Vildagliptin+ Metformin), various technologies like monolithic, bilayered, hot-melt extrusion, etc. may differ between the brand and generic products.<sup>[6]</sup>

Although generic drugs are always to be welcomed, it should not be at the cost of safety or therapeutic efficacy. Systems should be in place for pharmacovigilance, adverse event reporting, and constant surveillance of drug quality across batches. The results of BA/BE studies of approved generics should be published or available in the public domain for physician scrutiny.

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### Conflicts of interest

There are no conflicts of interest.

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