Is the switch from ethical to generic drugs safe and justified? No!

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As intellectual property protections are beginning to expire, cheaper generics for small molecule drugs (e.g. fingolimod), biosimilars for interferon-beta (IFN-β) and follow-on glatiramoids for the non-biologic complex drug (NBCD) glatiramer acetate (GA) are entering the vibrant market of MS therapies. In contrast to generics for small molecule drugs where only pharmaceutical equivalence and bioequivalence are required for demonstrating therapeutic equivalence, the greater complexity of biologics and the possibility of structural modifications and differences in bioavailability and immunogenicity introduced by manufacturing differences make their comparability to their innovator products more difficult, and may result in unpredictable differences in efficacy or safety. These complexities and the lack of appropriate regulation in some parts of the world may explain why several IFN-β biosimilars failed to show therapeutic or biological equivalence to their innovator products. Therefore, additional preclinical testing and properly conducted clinical trials are needed and strict regulation is essential. The NBCD GA is a heterogeneous mixture of potentially millions of distinct, synthetic polypeptides, which presents even greater degree of complexity as no two glatiramoid mixtures prepared by different manufacturers can be shown to be "identical". The innovative GA (Copaxone®) and several glatiramoids show some similarities using conventional methods, but also substantial differences in their physico-chemical properties, immunogenicity, gene expression, impact on biological pathways, safety profiles and most importantly – clinical efficacy. These differences should preclude their use as "generics" for GA, and call for more stringent regulations and carefully designed, comparative clinical trials to ensure the efficacy and safety of follow-on glatiramoids.