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Biosimilars and Generics: A New Class Needed for Hormonal and Herbal Preparations

ABSTRACT

Strict regulations are in place for the manufacture and approval of pharmaceutical products. Specific drugs such as biological products are governed by specific rules, which take cognizance of the extra diligence required for their production. This communication describes two classes of drugs: hormones and herbal products, which should be subject to stringent regulations. It explains the rationale behind this, and calls for added vigilance in regulatory oversight.

Keywords: Estrogen, good manufacturing practice, herbal products, hormones, pharmacovigilance, phytopharmaceutical, thyroxine

A vast multitude of pharmaceutical preparations exists today. With advances in technology, and with expanding industrial capacity, this number is increasing day by day. Regulatory authorities across the world try to keep pace with evolving needs and requirements by updating their guidance.

One such trend has been noted in the approval mechanism for biosimilars and generics. Classification of drugs as generics and biosimilars serves to differentiate chemical entities from biological products.^{1,2} This ensures that entities such as insulin, erythropoietin and monoclonal antibodies undergo a relatively stringent process of approval. While this is welcome, there is a need for a more comprehensive rubric to classify various drugs.

HORMONES

Various hormones and hormone mimetics used in the management of disease are classified as generic drugs; however, their production (manufacture), preparation (formulation) and presentation (storage) require specific and stringent conditions. These safeguards are necessary to ensure efficacy as well as safety. The production of

some hormones may lead to an endocrine disruptor effect, as metabolites of androgens and estrogens may act as endocrine disruptor chemicals if released into the environment.³ All tablets need excipients for stability, and some of these may be associated with adverse events. Thyroxine should be stored at a temperature not exceeding 25°C, and should be protected from light and moisture. Similar advice is suggested for desmopressin acetate.⁴

It makes sense, therefore, to reclassify hormones as non-generic drugs. Suggested terminologies, such as **steroid similars** (for dydrogesterone), **peptide products** or **peptide pills** (for desmopressin, semaglutide) **endocrine elixirs** (liquid thyroxine), **endocrine extracts** (desiccated thyroid extract) or **hormonal generics**, may help differentiate these medicinal products from simpler chemical entities (like paracetamol, for example), and allow tighter regulatory control.

This is important for both public health as well as individual clinical care. Stricter regulation will ensure avoidance of possible endocrine disruption at the manufacturing and distribution level, as well as ensure

Table 1. Precision and Perfection in Hormonal Products

- Pedigree: quality of manufacturing unit
- Procurement (of raw materials): from quality controlled sources
- Preparation: in uniform manner, following good manufacturing practices (GMP)
- Presentation: in environment-proof packaging

optimal cold chain networks. Most hormones have a narrow therapeutic index, (and are therefore known as Goldilocks hormones).⁵ Separate rules for regulatory approval will ensure that no substandard medications reach the public.

Particular attention should be paid to steroid hormones (dydrogesterone, micronized progesterone) and to peptides (desmopressin) while crafting new processes. Newer guidance should also keep in mind novel methods of formulation such as nanotechnology,⁶ which may influence the quality of hormonal medicinal products (Table 1).

HERBAL PRODUCTS

Another class of drugs, which needs regulatory advice is herbal products. Traditionally phytopharmaceuticals are regarded as safe, and are not subject to rigorous oversight. However, these too, are biological products, just as insulin and erythropoietin. This means that the concepts of biosimilarity and interchangeability, which apply to such medicines, should be applicable to herbal products or phytopharmaceuticals as well.

While multiple formulations of botanical extracts are available in the Indian market, it is doubtful that they will demonstrate equivalence in terms of pharmacodynamic or pharmacokinetic profiles.⁷ In fact, the inter-batch variability in phytopharmaceuticals is difficult to control even within the same manufacturing unit. This calls for a specific terminology for these medicinal products, too. 'Botanical biosimilars' or 'mineral-based medicinal' mimetics may be used to differentiate these

from simpler chemical entities, which can continue to be called generics.

SUMMARY

Our regulatory authorities exhibit a proactive and dynamic approach towards keeping their policies updated in tune with advances in the pharmaceutical and clinical arena. Attention needs to be paid, however, to various hormonal and phytopharmaceutical preparations, which have been currently re-clubbed in the 'generic' class of generic drugs. Understanding the heterogeneity of hormones, the nuances involved in their manufacture and the necessity for precise delivery of accurate dosage, will facilitate perfection in the process of endocrine drug development and marketing. This will be a valuable contribution towards achieving optimal endocrine health for all.

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