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The EU regulatory landscape of non-biological complex drugs (NBCDs) follow-on products: Observations and recommendations

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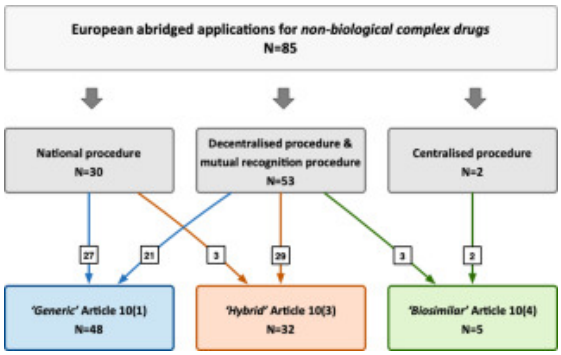
Abstract

"Non-biological complex drugs" (NBCDs), such as liposomal formulations, iron-carbohydrate complexes and glatiramoids, gained increased interest from a regulatory perspective in recent years. Similar to biologics, the quality of NBCD products is highly dependent on a robust and well-controlled manufacturing process. This provides challenges for generic drug developers to replicate NBCD products once market exclusivity of the originator product is expired. However, unlike biologics for which a consistent regulatory framework was established with the biosimilars pathway, NBCDs are not recognised as a distinct category of medicines and hence no formal regulatory pathway for their approval is defined. Currently, a "case-by-case" approach is applied for regulating NBCD follow-on products in the EU. Furthermore, NBCDs can follow a non-centralised authorisation procedure, leaving regulatory approvals to national competent authorities. This can lead to heterogeneity in the regulatory approach and outcomes when assessing NBCD follow-on products throughout the EU, which for some product classes has already resulted in some safety and efficacy implications. Here, we explore the regulatory landscape of NBCDs and their follow on products. This study shows that almost all of the 85 NBCD follow-on products available in the EU in 2018 have been approved via various non-centralised procedures. Although most NBCD follow-on products followed an Article 10(1) procedure, we clearly see a recent increase of the use of the hybrid pathway via Article 10(3). This study shows the heterogeneity in the regulatory approach taken for many NBCD follow on products. To what extent this may have consequences for their safety and efficacy evaluations is unknown and needs to be further investigated. The present study should stimulate the rethinking to design prudent regulatory pathways for NBCD follow-on products.

Graphical abstract



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Keywords

Non-biological complex drugs; Regulation; Equivalence; Generics; Drug approval; EMA; NBCD follow-on products

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