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Client Alert

FDA and Life Sciences

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European Commission Proposal Would Make It Harder for Innovator Companies to Launch Friendly Duplicates (Biosimilars)

The European Commission ("Commission") presented the results of the stakeholders' consultation on its "Note on Handling of Duplicate Marketing Authorisation Applications" ("Note on Duplicates") during the Pharmaceutical Committee meeting of November 2019. The Commission envisions erecting new barriers to limit the abilities of innovator manufacturers to launch duplicate (generic or biologic) versions of their own innovative products by requiring substantiation and sound evidence of increased availability in order to be authorized for marketing.

The Commission launched the consultation in May 2018 to learn about the potential impact of duplicate marketing authorizations ("duplicates") for "friendly" biosimilars, *i.e.* biosimilars developed by the innovators of the reference biological medicinal products and approved as generics[1], on the availability of biosimilars to healthcare professionals and patients.

Most national competent authorities ("NCAs")[2] that responded share the generic industry's concerns about the negative impact of friendly biosimilars on availability of biosimilars in the long run. The Commission therefore foresees amending the Note on Duplicates and requiring substantiation and sound evidence of increased availability of the product before authorizing a duplicate. Such modification would make it much more difficult to obtain duplicates of first friendly biosimilars – and the possibility of first friendly generics – and, as such, would impede the innovators' capacity to compete with companies manufacturing brand-competitive biosimilars.

ARTICLE 82(1) OF REGULATION 726/2004

The objective of the centralized marketing authorization procedure is to have, for each medicinal product, one marketing authorization ("MA") and one name valid throughout the European Union. Thus, Article 82(1), first indent of Regulation 726/2004, allows no more than one MA to be granted to a medicinal product authorized through the centralized procedure.

The second indent sets forth two exceptions: (i) when there are objective verifiable reasons relating to public health regarding the availability of medicinal products to healthcare professionals and/or patients ("public health") or (ii) for co-marketing. In such cases, the Commission may authorize one or more so-called duplicate MAs.

COMMISSION'S NOTE ON DUPLICATES

About ten years ago, the Commission issued the Note on Duplicates that further explains the two exceptions.

Basic Principles and Conditions. - Before defining the scope of application of the exceptions and detailing the authorization criteria, the Commission established a framework by stressing the basic principles, i.e., (i) assessment of each request on a case-by-case basis, taking into account the factual circumstances of each case; (ii) restrictive interpretation of Article 82(1), second indent; and (iii) importance of the objectives of preserving public health and harmonizing centrally authorized products.

Scope of Application – Same Medicinal Product and Same Applicant. - Article 82(1), second indent, address issues involving the "same medicinal product" (material scope) and a "same applicant" (personal scope) - two concepts that originate from the Commission's Communication on the Community marketing authorization procedures for medicinal products (1988).

Any medicinal products with the same qualitative and quantitative composition in active substance (i.e., the same strength) and the same pharmaceutical form, are to be considered as the same relevant product. The Note on Duplicates gives examples of cases when the Commission's prior authorization is required, including for friendly generics or biosimilars.

A company is deemed the "same entity" as a company that belongs to the same group of companies or as a company that has entered into a license agreement or has otherwise agreed to the marketing of the medicinal product. By way of example, the Commission stresses that Article 82(1) does not apply where an applicant is an independent company that entered into a license agreement, purchase agreement, or data agreement, with the MA holder of the product, but not for the placing of that product on the market.

DUPLICATES OF BIOLOGICAL MEDICINAL PRODUCTS

Issue. - Annex I.1 of the Note on Duplicates assumes that the first friendly generic, i.e., the first generic by the holder of the MA for the reference medicinal product, increases accessibility and thus availability of the product. The Commission, therefore, automatically authorizes a duplicate for the first generic of the innovator.

The Note on Duplicates, however, does not expressly refer to biological products and/or biosimilars, so that they are treated to the same as chemical products and generics.

Recently however, regulators started approving friendly biosimilars as generics, which has resulted in generic industry complaints that this practice could negatively impact national biosimilar markets. Only innovators can produce generics of their biological medicinal products and have them authorized through the abridged MA procedure (Art. 10(1) of Directive 2001/83). "Competing" biological products can only be characterized as "biosimilars" due to manufacturing/technological reasons and thus can only be authorized through the biosimilar MA procedure (Art. 10(4) of Directive 2001/83). The inability of being able to characterize competing biosimilars as "generics" has repercussions on factors that influence market access, including differences in the investment/development and authorization phases; eligibility for pharmacy substitution; clinical medical supervision; pricing policies; and tendering/procurement procedures.

Therefore, according to the generic industry, the introduction of a friendly biosimilar can initially have a positive effect on initial availability, but a negative long term effect, including paving the way for anticompetitive pricing practices.

Consultation. **–** Most respondent NCAs agreed with the generic industry's perspective, and all NCAs (except Hungary's) welcomed a revision of the Note on Duplicates. Their position, however, is only based on theory, as there is not yet any experience or evidence on the actual effect of friendly biosimilars on availability of biosimilars to healthcare professionals and patients.

In the Consultation, the Commission suggested that requests for duplicates be properly substantiated and based on sound evidence. Almost all respondents agreed on the need for more clarity on what "properly substantiated" and "sound evidence" actually entails, as well as on the various terms used.

REVISIONS TO THE NOTE ON DUPLICATES

The Commission is now considering amending Annex I.1. of the Note on Duplicates and has submitted the following possible changes to the Member States for discussion:

A duplicate MA is an exceptional process.

For duplicates (chemical or biologic) requested on the basis of public health reasons, the applicant should provide specific evidence with regard to the product to allow the Commission to verify a positive effect on availability.

Taking into account the experience gained with market realities, the first entry of a generic on the market is not automatically assumed to increase availability.

The applicant should justify why a duplicate is needed and demonstrate how a second MA would increase availability and patient access, based on objective and verifiable reasons. In this regard, one possibility is to ask the applicant, as part of their justification for increased availability and patient access, to list the Member States where the "first" medicinal product is actually marketed and indicate where the duplicate will be made available. If the market intention does not cover the entire EU, justification should be provided and the Member States in which the product is not to be placed on the market should be listed.

It is unclear whether the Member States will share the Commission's approach, but the results of the Consultation suggest that they will.

COMMENTS

The Commission's proposal, if adopted, would raise significant hurdles for the authorization of first friendly biosimilars forcing the innovator to demonstrate an increased availability of the product, being understood that a lower price alone is not sufficient proof of availability. The same requirement will most likely apply to first friendly generics as well.

In spite of the apparent policy goals behind the proposal for incentivizing long-term access and reduced pricing, there are at least three ways in which the proposal could be challenged. First, the legal basis for the approval of friendly biosimilars is presented as the genesis of the issue – it is the generic status of the friendly biosimilar that influences market access factors. Yet, the proposal does not address the problem because a duplicate for a friendly biosimilar would be authorized, even if it were to influence market access factors.

Second, the proposal would de facto require innovators to place their friendly biosimilars on more national markets; otherwise competition would be thwarted, as competing biosimilars would immediately dominate the market. Indeed, in many instances, the national measures designed to boost generics resulted in reference products no longer being prescribed by doctors or dispensed by pharmacists, despite drastic price decreases. The situation will most likely be the same for biosimilars, once similar boosting measures are adopted or applied and healthcare professionals' reluctancy to switch patients to other biological products vanishes. Given the national boosting measures, friendly generics and biosimilars are often the only options left to innovators to continue marketing their own products. This option would now

be conditioned on a broader marketing of friendly biosimilars, which may otherwise not be in the interests of the innovators.

Third, as the innovative industry explained during the Consultation, substantiating and bringing sound evidence of increased availability would be very difficult in practice, especially if a price decrease is insufficient to demonstrate increased access in and of itself. No express measures exist today.

Overall, the real issue seems to be interchangeability. Friendly biosimilars otherwise are in the same situation as friendly generics, except for healthcare professionals' reluctancy to prescribe and dispense competing biosimilars because they are not exact copies and patient interactions are necessarily unknown for a period of time. If competing biosimilars were as regularly and easily prescribed and dispensed as competing generics from the time of authorization, the risk of the friendly biosimilar impeding the availability of biosimilars would be very limited. The solution, therefore, may be to adopt clear interchangeability guidelines or to educate healthcare professionals and patients in biosimilars rather than to limit innovators' ability to compete or market.

Moreover, we note a possible link with the ongoing discussion on the actual marketing of centrally approved medicinal products. Certain Member States have complained that many centrally authorized products are not sold on their national market. The problem, which results from many factors (in particular lack of sufficient patient population and international reference pricing), cannot be resolved through the sunset clause because it currently is interpreted as requiring only the actual marketing of one presentation in one national market, The Commission is looking into the issue, and subjecting duplicates to an extended marketing of friendly biosimilars could be part of the solution.

Friendly generics and biosimilars are keys for innovator companies to compete in Europe after the protections on their medicines have expired. King & Spalding's experienced European regulatory and competition lawyers regularly work with branded pharmaceutical companies, including on strategies for their innovator products. Our lawyers assist with requesting and justifying duplicates for friendly generics and biosimilars, as well as with disputes involving the European Commission's application of Article 82 of Regulation 726/2004, including before the Courts of Justice of the European Union.

[1] The Commission refers to friendly biosimilars as "autobiologicals".
[2] Belgium, Denmark, Spain, Finland, France, Hungary, the Netherlands, Portugal, Sweden.