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Short communication

The interpretative evolution of Article 10b

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Introduction

Fixed-dose combinations (FDCs) integrate two or more active substances into a single dosage form, aiming to improve patient adherence and achieve synergistic therapeutic effects. Article 10b of Directive 2001/83/EC establishes a regulatory pathway for such products which allows applicants to rely on existing data for the individual components, supplemented by new pre-clinical and/or clinical data relating to the combination. (European Commision, 2019).

Recent case developments reveal increasing interpretative tension surrounding Article 10b. In particular, the provision's open wording has led to divergent approaches among National Competent Authorities (NCAs), especially concerning what constitutes "new" data sufficient to justify exclusivity.

The EU pharmaceutical reform (the Pharma Package) is a major legislative overhaul finalized in late 2025 designed to replace 20-year-old rules with a modernized, unified regulatory framework, expected to become fully applicable by 2028 following a transition period. The new pharmaceutical legislation is designed to adapt the EU regulatory framework to support and foster innovation. New incentives will encourage companies to make their medicines available to patients, earlier availability of generic medicines will be facilitated, and market authorization procedures simplified. (European Commission, Reform of the EU pharmaceutical legislation)

The bioequivalence paradox

A key point of contention arises where an Article 10b application is supported solely by bioequivalence (BE) studies. Under the Commission's Notice to Applicants, such studies are typically regarded as "bridging" evidence: they demonstrate comparable pharmacokinetic behavior rather than generating new therapeutic knowledge. On this basis, BE studies would not ordinarily meet the threshold required to trigger data exclusivity.

The issue becomes more complex in practice. In cases such as Vabinxo®, certain NCAs have granted the full (8+2) exclusivity period despite the application relying primarily on BE data. (Public Assessment Report, Vabinxo® 2014).

This approach exposes a fundamental divergence in regulatory practice. On one hand, it supports lifecycle innovation by incentivizing the development of new combinations. On the other, it raises concerns regarding regulatory consistency. Products supported by minimal clinical evidence may obtain the same level of protection as those backed by extensive therapeutic data, potentially distorting competitive dynamics.

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By endorsing a broader interpretation of Article 10b, BE studies - by virtue of being newly conducted Phase I clinical trials - are sufficient to satisfy the requirement for “new clinical data.” By enabling FDCs supported solely by BE data to qualify for full exclusivity, the NCAs risk blurring the critical distinction between substantive clinical development and the technical demonstration of equivalence.

Divergent national approaches

There is a pending request for a preliminary ruling from the Dutch Raad van State (Council of State) lodged on December 30, 2025. The case C-877/25 centers on whether Article 10b of the EU Medicinal Products limits the regulatory pathway for fixed-dose combinations to a single applicant. The Court’s ruling will determine if first-to-file companies gain a de facto monopoly over this simplified route, impacting market entry for subsequent competitors.

In case C-877/25, a ruling that Article 10b can be applied multiple times would allow subsequent applicants to rely on existing data for individual substances without repeating pre-clinical and clinical studies.

Conversely, if the Court limits Article 10b to a single use per combination, competitors would face significant barriers, being required either to submit a full dossier under Article 8 (3) or to wait until the expiry of the protection period.

Conclusion

While Article 10b remains a vital mechanism for expanding therapeutic options through combination products, its practical impact is being tested by legal ambiguities regarding exclusivity and data requirements.

The European Parliament and the Council of the European Union have reached political agreement on the reform of the EU pharmaceutical legislation on 11 December 2025. The following two years, until 2028, will serve as a transition period during which Member States must implement the new Directive into national law and adapt regulatory practices accordingly (European Commission, Reform of the EU pharmaceutical legislation). However, the success of these reforms will depend not only on legislative alignment but also on achieving greater consistency in regulatory interpretation across NCAs. To fully realize the potential of Article 10b and support the development of clinically meaningful FDC therapies, future regulatory refinement should prioritise harmonization of NCA decision-making and aligning the interpretation of "new scientific data." Establishing the uniform criteria would reduce regulatory fragmentation, encourage investment, and ultimately enable promoting public health outcomes without creating unnecessary hurdles for market competition.

It remains to be seen whether, over the course of this two-year transitional period, generic manufacturers will capitalize on the opportunity for market monopoly by adopting the more complex strategies of originator companies.

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