EU pharmaceutical reform: the ESC outlines key priorities for trilogue

The European Society of Cardiology (ESC) welcomed the adoption of the Council's position on the reform of the EU Pharmaceutical Legislation as a significant and long-awaited step forward. However, we highlight several critical shortcomings that must be addressed as interinstitutional negotiations (trilogues) begin.

A core concern for the ESC is the limited and optional nature of **consultation with healthcare professional organisations** across key provisions of the text. This marks a step back compared to the European Parliament's position, which had strengthened stakeholder engagement for good reasons throughout the regulatory lifecycle.

As the first point of contact for patients and a bridge between clinical practice and regulation, healthcare professionals, such as represented by the ESC, can contribute significantly to various regulatory processes, by sharing their expertise and insights from real-world clinical practice and scientific evidence alike. We therefore call on EU policymakers to ensure their active involvement in the regulatory system is reflected in the reform. This should build on the positive experience of stakeholder engagement and targeted consultations by the European Medicines Agency, as well as by the European Commission within key legislative frameworks including the Health Technology Assessment Regulation, the European Health Data Space, and the Medical Device Regulation.

For the same reasons, we believe that the voting rights of healthcare professionals and patient representatives during the Committee for Human Medicinal Products' deliberations, which are removed by article 148a, should be preserved.

Below is a summary of other key recommendations by the European Society of Cardiology.

Unmet Medical Needs (UMN) (Article 83, Directive)

The ESC calls on policymakers to adopt an inclusive definition of Unmet Medical Needs (UMN) that fully reflects the real-world burden of disease and patient needs.

- The new criterion proposed by the Council remains vague, lacking a clear definition of what constitutes a "clinically relevant improvement." As criteria are expected to be clarified in scientific guidelines to be developed by the European Medicines Agency (EMA), healthcare professionals must be actively involved in this process. While the European Parliament's position includes stakeholder consultation, the Council's text does not. Clinical experts possess first-hand experience in patient care and a deep understanding of the limitations of current therapies based on solid scientific evidence. Their insights are vital to ensuring that UMN criteria are grounded on scientific evidence, real-world clinical practice and aligned with patient needs. Their involvement must therefore be a priority in a professional development of such guidelines. This has already been the case for the development of

regulatory guidelines on orphan and breakthrough medical devices, so we call regulators to follow the same inclusive consultation model.

- The definition also overlooks critical dimensions such as disease burden and patient-centered factors, like quality of life and treatment-related adverse effects. These elements are essential for a comprehensive assessment of the real-world impact of a condition and the limitations of current therapies. The Directive should explicitly require that such factors be considered when assessing unmet needs.

Transparency (Article 57, Directive)

Enhanced transparency on public financial support received for R&D costs can positively contribute to pricing and reimbursement processes and therefore to the sustainability of health systems. The extension to indirect funding and information on products licensed or acquired from other entities provided in the Parliament's position should be supported.

PRIME scheme (Article 60, Regulation)

The requirement for "exceptional therapeutic advancement" lacks specificity and should be clarified via scientific guidelines developed in consultation with relevant stakeholders, including healthcare professionals and patient organisations. In addition, the focus on rarity or novelty alone is too narrow and may exclude treatments with high public health value. In this respect, it is noteworthy that out of 384 PRIME requests submitted to the European Medicines Agency (EMA) between 1 January 2016 and 30 June 2021, only 20 concerned cardiovascular disease - despite it being the leading cause of death in Europe - and just 2 were granted eligibility to the scheme[1]. This highlights a significant gap in support for innovation in high-burden, high-mortality areas. Expanding the scope of the PRIME scheme to include chronic diseases or conditions associated with substantial mortality and morbidity and for which drug approval remains limited despite the significant disease burden would deliver tangible benefits to European patients and strengthen the resilience of health systems across the European Union.

Medicine shortages (Chapter X, Regulation)

While the ESC welcomes the inclusion of "medicines that may become critical due to supply vulnerabilities" in the definition of the Union List of Critical Medicines, the role of healthcare professionals in the prevention and management of shortages is underrepresented:

- *Identification of critical medicines*: with respect to the methodology to be developed by the EMA, the wording "in consultation, where appropriate, with relevant stakeholders" is insufficient. Healthcare professionals should be consulted throughout the process and included before the adoption of the final list, as they can offer key insights on the therapeutic

[1] Piotr Szymański, Faiez Zannad, Thomas F Lüscher, Urgent need to define unmet medical needs in cardiovascular diseases, *European Heart Journal*, Volume 45, Issue 16, 21 April 2024, Pages 1384–1385, https://doi.org/10.1093/eurheartj/ehae041

relevance of treatments in alignment with scientific evidence as well as clinical practice guidelines and on the adequacy of alternatives, also based on previous or ongoing local shortages (art. 30.1).

- *Shortage prevention plans*: we call on policymakers to maintain the Parliament's provision to consult the Healthcare Professionals' Working Party and the Patients' and Consumers' Working Party in the development of guidance on shortage prevention plans within the final text (art. 117.2).

- *Information sharing:* the Parliament introduced a positive information exchange between regulators and stakeholders in the management of shortages which should be maintained, as follows.

    - National competent authorities tasked to:
        - Collect and assess information on potential and actual shortages provided by a series of actors, including healthcare professionals, patients and consumers (art. 121.1)
        - Ensure that information on ongoing shortages, including expected duration and available alternatives, is actively communicated to representatives of healthcare professionals and patients (art. 121.2) and published on national websites on medicines shortages (art. 121a).
    - The EMA is tasked to consult the Healthcare Professionals Working Party and the Patients and Consumers Working Party in the listing, monitoring and management of critical shortages (art. 122.4 – Am. 274).

Another gap in the Council's text concerns **joint procurement of medicinal products**, which is limited to the high-level reference to the Joint Procurement Agreement in the Commission's proposal. Also in this case, the Parliament had gone a step further, entitling the Commission to facilitate joint procurement of centrally authorised medicinal products at Union level on Member States' behalf, by defining conditions and procedures via delegated acts (article 73a). Extending joint procurement - beyond critical medicines under the recent proposal for a Critical Medicines Act - would enhance equitable access and help reduce costs, benefiting patients across Europe.

Repurposing (Art. 48, Regulation)

The ESC welcomes the Council's decision to extend the possibility of submitting evidence to regulators for new therapeutic indications to include medicines beyond those targeting unmet medical needs, aligning with the position of the European Parliament. However, it remains unclear why Article 48.2 restricts the updating of product information solely to cases of unmet medical need. Such a limitation appears inconsistent with the broader aim of encouraging repurposing, which can expand access to treatments and deliver substantial benefits to patients. To fully realize the potential of repurposing, the scope should be more inclusive. At the same time, we call for legislators to ensure

that if a product receives a new therapeutic indication, access for well-established uses is not hampered by unduly price increases, like occurred in the case of mexiletine[2].

Added therapeutic value (Art. 153, Regulation)

To ensure that real-world perspectives and clinical relevance are reflected in the EMA guidelines on added therapeutic value, we call for healthcare professional and patient organisations to be consulted by regulators, as defined by the European Parliament. We also call for the inclusion of evidence generated through publicly funded registries and real-world data analyses conducted by healthcare professionals as an integral part of the process, leveraging the European Health Data Space as a key enabler.

Redispensing of medicines (Article 207a, Regulation)

While supportive in principle, we stress that redispensing must be accompanied by rigorous safeguards: EU-wide traceability systems, eligibility criteria for safe reuse, and clear exclusion of high-risk or unstable products. Informed consent is also essential.

In brief, the ESC urges policymakers to ensure that the Reform of the EU Pharmaceutical Legislation establishes a future-proof framework that reflects the realities of clinical practice, addresses the needs of patients, and is informed by real-world insights and collaborative policymaking.

[2] 7 Pieter G Postema, Peter J Schwartz, Elena Arbelo, Wilbert J Bannenberg, Elijah R Behr, Bernard Belhassen, Josep Brugada, Pedro Brugada, A John Camm, Ruben Casado-Arroyo, Ellen 't Hoen, Carla E M Hollak, Stefan Kääb, Pier D Lambiase, Antoine Leenhardt, Silvia G Priori, Vincent Probst, Bas C Stunnenberg, Jacob Tfelt-Hansen, Baziel G M Van Engelen, Christian Veltmann, Sami Viskin, Arthur A M Wilde, Continued misuse of orphan drug legislation: a life-threatening risk for mexiletine, European Heart Journal, Volume 41, Issue 5, 1 February 2020, Pages 614–617, https://doi.org/10.1093/eurheartj/ehaa041