Macedonian Pharmaceutical Bulletin, 72 (Suppl 1) 283 - 284 (2026)
Online ISSN: 1857-8969
DOI: 10.33320/maced.pharm.bull.2026.72.03.136
Short communication

The modernization of orphan drug regulation and its impact on patients' quality of life

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Introduction

Rare diseases represent a significant global health challenge because, although each individually affects a small number of patients, their cumulative prevalence is high. Patients with rare diseases often face limited access to appropriate therapies, and orphan drugs are often the only option for improving quality of life and clinical outcomes. However, the development, import, and distribution of these medicines are complex processes that require strict regulatory control and robust quality assurance systems. Ensuring quality in the supply chain of orphan drugs is critical, not only from an industrial perspective but also from a patient-centered point of view, as any delay or shortage may directly compromise therapy continuity and patient well-being. In this context, the present study analyzes key regulatory frameworks for rare diseases, examines quality assurance processes in the import and distribution of orphan drugs, evaluates their impact on patient access, and proposes strategies to improve transparency and availability (EMA, 2018; EC, 2026; eupp, 2025; PRGRD, 2025).

Materials

This study is based on a qualitative regulatory and comparative analysis. It reviews the European Union framework for orphan drugs, including Good Distribution Practice (GDP), Good Manufacturing Practice (GMP), and import authorization requirements (MIA). Furthermore, a comparative analysis between EU and North Macedonian regulatory systems was conducted to assess levels of alignment, identify gaps, and highlight challenges. A case-based approach focusing on Wilson's disease was also included in order to evaluate the real-world implications of regulatory mechanisms on therapy continuity and patient care. (EC, 2026; Dir. 2001/83/EC, 2011; PPNM, 2024).

Discussion

The analysis demonstrates that European Union operates a well-established and harmonized regulatory system that ensures high standards of quality, safety, and availability of orphan drugs. In contrast, North Macedonia shows partial alignment with EU standards, with notable improvements following regulatory reforms implemented in 2018, particularly in the areas of quality control and

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pharmacovigilance. Despite these advancements, key challenges remain, including the absence of a dedicated orphan drug framework, limited access to therapies, financial constraints, and reliance on centralized procurement systems. While stricter regulatory control has improved patient safety and reduced risks such as falsified medicines, administrative procedures and supply chain limitations may lead to delays and interruptions in therapy. This is particularly critical for patients requiring lifelong treatment, such as those with Wilson's disease. The findings emphasize the need for greater regulatory harmonization, more flexible procurement mechanisms, and implementation of innovative approaches such as Health Technology Assessment (HTA) and managed entry agreements. (EUPP, 2025; HTA Reg, 15; PPNM, 2024)

Conclusion

Ensuring timely, safe, and equitable access to orphan medicines remains a major challenge for patients with rare diseases. Recent regulatory developments in North Macedonia have improved quality assurance and patient safety. However, further alignment with European Union standards is needed to enhance the availability and continuity of treatment. Strengthening health technology assessment processes, procurement mechanisms, pharmacovigilance, and regional cooperation can contribute to more sustainable access to orphan medicines. In parallel, ongoing efforts to develop a national strategy for rare diseases, initiated by patient organizations, represent an important step toward addressing unmet patient needs and improving health outcomes and quality of life for people living with rare diseases.

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