Macedonian Pharmaceutical Bulletin, 72 (Suppl 1) 461 - 462 (2026)
Online ISSN: 1857-8969
DOI: 10.33320/maced.pharm.bull.2026.72.03.222
Short communication

Pragmatic approaches and evaluation of effectiveness of additional risk minimization measures

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Introduction

Pharmacovigilance is a key public health discipline focused on the detection, assessment, understanding, and prevention of adverse drug reactions (ADRs). The need for robust pharmacovigilance systems emerged following historical safety incidents such as the thalidomide tragedy. However, pre-authorisation clinical trials are conducted in limited populations and under controlled conditions, making post-marketing surveillance essential for identifying previously unknown or rare risks (EMA, 2017; ICH, 2004). Risk minimisation measures (RMMs) are interventions designed to optimise the benefit–risk balance of medicinal products. These include routine measures, such as product information and labelling, and additional risk minimisation measures (aRMMs), which are implemented when routine measures are insufficient. aRMMs aim to prevent or reduce the occurrence and severity of ADRs through targeted interventions such as educational materials, controlled access programmes, and patient monitoring tools. Given the dynamic nature of the benefit–risk balance throughout the lifecycle of medicinal products, continuous evaluation of effectiveness is essential.

Materials and methods

This work is based on a structured review and analysis of international and European pharmacovigilance frameworks, including ICH E2E guidelines, CIOMS IX recommendations, and EU Good Pharmacovigilance Practices (GVP), particularly Module XVI (EMA, 2021; EMA and HMA, 2015; EMA and HMA, 2024a; EMA and HMA, 2024b). The analysis includes regulatory approaches from several regions (EU, USA, Canada, Australia, Japan, and the UK), as well as national implementation in North Macedonia. Various aRMM tools were examined, including educational materials for healthcare professionals and patients, patient alert cards, controlled access and distribution systems, pregnancy prevention programmes (PPP), and direct healthcare professional communication (DHPC). Effectiveness was evaluated using process indicators (awareness and distribution), behavioural indicators (changes in prescribing and use), and outcome indicators (reduction in ADRs) (EMA, 2021; EMA

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and HMA, 2015; EMA and HMA, 2024a; EMA and HMA, 2024b)

Results and discussion

RMMs are essential components of pharmacovigilance systems, with routine measures applied universally, while aRMMs are introduced for medicines with specific safety concerns. Educational programmes represent the most common aRMM tool, targeting both healthcare professionals and patients. Other measures include controlled distribution systems, patient registries, and pregnancy prevention programmes. These interventions are designed to influence knowledge, behaviour and ultimately clinical outcomes. Despite initial educational measures, continued exposure during pregnancy led to the introduction of stricter programmes, including PPP and patient cards, demonstrating the need for continuous adaptation. Implementation at national level requires coordination between regulatory authorities and marketing authorisation holders. In North Macedonia, the Agency for Medicines and Medical Devices (MALMED) aligns with EU standards, ensuring local adaptation, approval, and monitoring of aRMMs. Evaluation studies indicate that while awareness may improve, impact on clinical outcomes is sometimes limited, highlighting the need for robust methodologies and continuous monitoring (CIOMS, 2014; EMA, 2017).

Conclusion

Additional risk minimisation measures are critical tools for ensuring the safe and effective use of medicines, particularly for products with significant risks. Their success depends on appropriate design, targeted communication, and integration into clinical practice. Continuous evaluation using robust methodologies is essential to assess their effectiveness and guide improvements. The alignment of national systems with EU pharmacovigilance standards strengthens risk management capacity and contributes to improved patient safety. A dynamic and evidence-based approach remains essential throughout the lifecycle of medicinal products.

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