HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

# Optimising the safe and effective use of medicines in clinical practice through proactive risk management

Through the EU system of pharmacovigilance, national competent authorities such as the HPRA, coordinated by the European Medicines Agency (EMA), oversee the assessment of the benefit and risks of medicines throughout the product lifecycle, with proactive planning and management of risks from the time of first authorisation through to use in clinical practice. A key aim of pharmacovigilance is to optimise the safe and effective use of medicines through the provision of evidence based recommendations to healthcare professionals and patients to minimise risk.

For each authorised medicine, there is a risk management plan, through which there is proactive planning to reduce the burden of adverse reactions on patients and to optimise clinical benefit. Typically, risks relating to medicines are adequately addressed using routine risk minimisation measures, such as information and advice contained in product information (Summary of Product Characteristics (SmPC) and Package Leaflet (PL)), packaging or labelling, and through the method of sale and supply (e.g. prescription-only).

However, when routine measures alone are not considered sufficient to address an important safety issue for a particular medicine, additional risk minimisation measures are recommended as a complement to product information. Additional risk minimisation measures focus on the most important, preventable risks, with the feasibility and impact on the health system of implementing additional risk minimisation carefully balanced with the anticipated benefit for patients.

Additional risk minimisation measures can include Direct Healthcare Professional Communications (DHPCs) and/or educational materials. DHPCs are used to deliver important safety information directly to a healthcare professional (HCP). The pharmaceutical company that holds the licence for the medicine, following approval by the HPRA, distributes DHPCs in Ireland. All DHPCs are published on the HPRA website.

Educational materials usually focus on one or more specific safety concerns (e.g. hepatotoxicity, cardiovascular risk, teratogenicity) related to use of that medicine and provide clear information on the nature of the specific risk(s) and actions required to prevent and/or minimise the risks, thereby optimising the risk-benefit balance for patients. Educational materials and tools may be intended for HCPs (e.g. doctors, pharmacists and nursing staff) and/or be made available to HCPs to provide to patients and caregivers.

Examples of educational materials for HCPs include healthcare professional guides, dosing and administration guides, prescriber checklists and monitoring charts. These may outline considerations before prescribing, e.g. prescriber checklist for combined hormonal contraceptives (to minimise the risk of venous thromboembolism), or the prescriber guide for rivaroxaban (to minimise the risk of bleeding). Other examples include measures taken to minimise the risk of exposure of children in-utero to teratogenic medicines in the form of pregnancy prevention programmes, e.g. valproate (the 'prevent' programme), systemic retinoids and thalidomide. In other cases, specific monitoring may be required while a patient is on a medicine, to detect early signs of the occurrence of potentially serious adverse reactions (such as monitoring liver function for patients on agomelatine to minimise the risk of hepatic injury).

Educational materials are also used to remind patients about important safety information that they need to be aware of to use medicines safely and effectively. They may also highlight circumstances where patients need to seek medical advice. Examples of educational materials for patients include patient alert cards (e.g. Eliquis), patient guides (e.g. Epilim▼) and patient reminder cards (e.g. methotrexate to remind patients of once weekly dosing in certainindications). It is important that HCPs prescribing these medicines ensure that patients are aware of these materialsand are provided with copies of them.

This field is continuously developing, with advances such as interactive web-based tools likely to gain prominence in addition to the paper-based educational materials. Research into the effectiveness of such tools plays a fundamental part in medicine risk management and can inform the need for new or amended measures, as well as identify when specific tools may no longer be needed.

Educational materials are produced and distributed by the Marketing Authorisation Holder (MAH) of the medicine only when it is a requirement of the Risk Management Plan for that specific product. The necessity for this and the materials themselves are agreed and approved by the HPRA as part of the assessment of the Risk Management Plan. In Ireland, risk minimisation tools are typically produced in hard copy format, and distributed by the MAH by post to an agreed target HCP audience (which may be e.g. GPs, specialists, pharmacists). On average, risk minimisation tools are distributed for 20-40 medicines annually. For tools to be effective, it is essential that HCPs are aware of their importance when received and that they take the necessary steps to implement the risk minimisation advice in their clinical practice and provide their patients with any patient-focused educational materials as appropriate.

HPRA approved educational materials are listed on the HPRA website and can be readily accessed and downloaded for use by HCPs and patients. Further information for a specific medicine may be found on www.hpra.ie, using the 'Search for a Medicine' function. The tools appear under the documents column of the product listing (EdM), together with Summary of Product Characteristics (SmPC) and Patient Information Leaflet (PIL). For a full list of medicines that have Educational Materials use the advanced search option and click on 'Only Medicines with Educational Materials'.