

# HPRA DRUG SAFETY

## NEWSLETTER

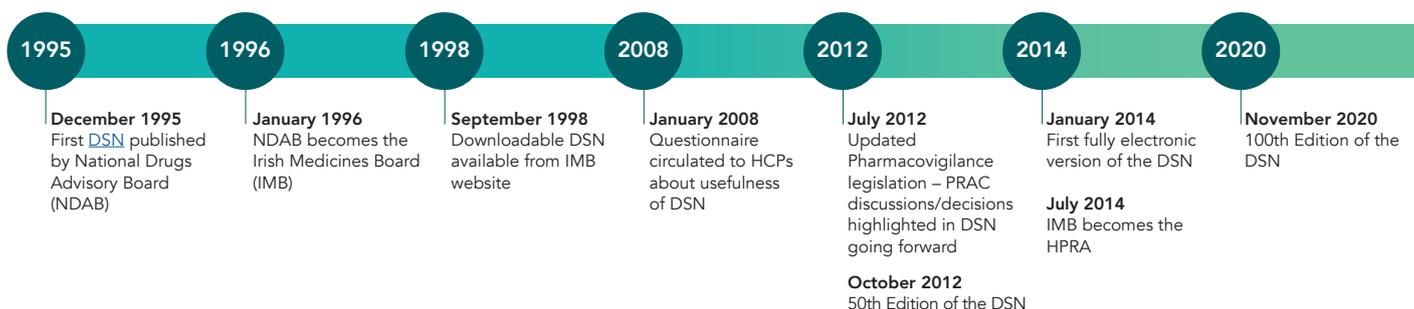
100<sup>TH</sup>  
EDITION

## Welcome to the 100<sup>th</sup> Edition of the HPRA Drug Safety Newsletter

For many people, taking medicines is a regular part of their daily life and these medicines are relied on to treat disease and improve health. While medicines provide enormous health benefits, no medicine is without risk. As highly regulated healthcare products, medicines are authorised only when it is judged that the product concerned is of high quality and that the benefits outweigh the potential risks. Once a medicine is authorised and placed on the market, monitoring of the benefits and risks continue throughout its lifecycle through a system known as pharmacovigilance.

In this edition, coinciding with the COVID-19 pandemic, we highlight the importance of continued reporting of suspected adverse reactions associated with medicines, including those used in the treatment of COVID-19, together with articles on optimising the safe use of medicines through risk minimisation interventions, access to approved and up to date product information, and registering with the HPRA for alerts.

This special 100th edition of the Drug Safety Newsletter (DSN) includes an article written by the HPRA's Pharmacovigilance Manager, Ms. Niamh Arthur, on the role of the DSN since its initial publication in 1995.



## 'The goals of the DSN – the same in 1995 as today' writes Ms. Niamh Arthur, Pharmacovigilance Manager

In 1995, when the first edition of the Drug Safety Newsletter (DSN) was published, it was intended as an occasional publication to communicate new and emerging pharmacovigilance issues to physicians and pharmacists. The frequency of publication of the DSN increased steadily over time with approximately six editions now issued annually. The DSN is also now distributed to an increasing audience of healthcare professionals, primarily through their professional organisations, as well as to specific patient organisations, as relevant topics arise. The DSN is published on the [HPRA website](#), where historical editions can also be located.

Marking the 100th edition of the DSN is an important milestone, spanning a twenty-five year period in which we have seen many changes in the field of therapeutics, including the development of new, innovative and targeted treatments, along with developments in the regulatory framework to support and enhance patient safety.

The HPRA's intention for the DSN has been to provide clear and concise communications on safety issues with medicines directly to healthcare professionals and after 25 years, it remains a conduit for the provision of this information, ensuring that the latest data and updated recommendations to support safe use of medicines are highlighted, in line with our remit to protect public health.

## Working with Healthcare Professionals

Healthcare professionals play a crucially important role in pharmacovigilance and their willingness to report suspected adverse reactions is and will continue to be the cornerstone of drug safety systems. There are many examples where an observant healthcare professional has alerted regulators to an emerging safety signal and we continue to work in partnership with healthcare professionals to encourage reporting of adverse reactions observed in their practice.

The role of healthcare professionals in supporting pharmacovigilance efforts is not however, confined to the reporting of adverse reactions - a key aspect is their role in communicating and managing risk at the individual patient level. Through the DSN and other materials available on the HPRA website, healthcare professionals can access up to date information on medicines.

The publication of the DSN over the past 25 years involves considerable time and effort, with many of the staff in the Human Products Monitoring Department of the HPRA contributing to it through their respective roles, from identification of topics for inclusion, to drafting and review of articles, editing and finalising texts, liaising with stakeholders, typesetting and distribution.

The HPRA strives to ensure that the DSN can be considered as a relevant and trusted source of information for medicines and one that continues to meet the needs of healthcare professionals in an increasingly complex and overloaded communications environment. We are committed to continuing to work in partnership with healthcare professionals to achieve our overall objective of promoting and protecting public health and, in this context, encourage you to continue to provide your comments and feedback on the contents of the publication.

### In this Edition

- Optimising safe and effective use of medicines in clinical practice through proactive risk management
- Adverse reaction reporting
- Product information for medicines
- Registering with the HPRA for safety alerts and updates

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

Medicines are subject to ongoing assessment of benefit and risks, from the time of first authorisation and then periodically thereafter over their lifecycle. Through risk management, regulators aim to support healthcare professionals and patients optimise the safe and effective use of medicines.

Through *risk management plans*, 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, packaging or labelling and through the method of sale and supply (e.g. prescription-only). However, when routine measures are not considered sufficient for some key safety concerns for a particular medicine then *additional risk minimisation measures* are required. These usually consist of *educational materials* that focus on one or more specific safety concerns (e.g. hepatotoxicity, cardiovascular risk, teratogenicity) related to use of the medicine. These provide clear information on the nature of specific risks and actions required to prevent and/or minimise such risks and thereby, optimising the risk-benefit balance for patients.

Additional risk minimisation measures focus on the most important, preventable risks, with the burden of imposing additional risk minimisation on the health system carefully balanced with the benefit for patients. Educational materials and tools may be intended for healthcare professionals (HCPs e.g. doctors, pharmacists and nursing staff) and/or patients and caregivers.

Types 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 rivoraxaban (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. sodium 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 liver function test (LFT) monitoring for patients on agomelatine to minimise the risk of hepatic injury).

Educational materials for patients are intended to remind 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, patient guides and patient reminder cards. It is important that HCPs prescribing these medicines, ensure that patients are aware of these materials and have a copy 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 identifying 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 a target HCP audience (which may be GPs, specialists, pharmacists, etc.). On average, risk minimisation tools are distributed for 20-40 medicines annually.

For risk minimisation tools and educational materials to be effective, it is essential that HCPs are aware of their importance. It is important that on receipt of these materials, the necessary steps are taken to implement the risk minimisation advice into clinical practice and to provide 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](http://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 Package Leaflet (PL). For a full list of medicines that have Educational Materials use the advanced search option and click on 'Only Medicines with Educational Materials'.

## Adverse Reaction Reporting

The HPRA greatly appreciates, and depends upon, the contribution to the spontaneous reporting of suspected adverse reactions by busy healthcare professionals (HCPs). Information collected through this system is an important method of monitoring medicine/vaccine safety in normal clinical practice, by increasing knowledge about known adverse reactions and also by acting as an early warning system for the identification of previously unrecognised adverse reactions. Such information is one of the tools used by the HPRA and other regulators in the ongoing safety evaluation of medicines post authorisation.

The HPRA welcomes initiatives to support and encourage reporting including the recent medication safety week (02/11-08/11/2020), which was an international campaign led by Uppsala Monitoring Centre (UMC), the World Health Organisation's (WHO) Collaborating Centre for International Drug Monitoring. A key focus of this campaign was 'Every report counts' (See Figure 1) and further information on this campaign is available [here](#).

When reporting suspected adverse reactions, as much as possible of the following information should be provided (however, please note that non-availability of all this information should not discourage report submission):

- Information on the **patient** who has experienced the side effect, including age (or age group) and sex, and any additional available information such as weight/BMI, pregnancy status, co-morbidities etc.
- A description of the **suspected adverse reaction**, including clinical course, and outcome where known;
- The **name of the medicine** (brand name as well as active substance) suspected to have caused the adverse reaction;
- Dose and duration of treatment with the medicine;
- The batch number of the medicine administered (essential for reports involving biological medicines);
- Any concomitant medications (including non-prescription medicines, herbal remedies or contraceptives);
- **Reporter** (HCP or patient) details.

The full range of reporting options can be found at [www.hpra.ie/report](http://www.hpra.ie/report). However, at present when the majority of staff are working remotely due to the COVID-19 pandemic, wherever possible, HCPs, patients, and caregivers are asked to submit all reports of suspected adverse reactions electronically via the online reporting system (accessible [here](#)) (See Figure 2), or by email to [medsafety@hpra.ie](mailto:medsafety@hpra.ie).

Additionally important at this time, the HPRA and European Medicines Agency (EMA) are requesting HCPs caring for patients with confirmed or suspected coronavirus disease (COVID-19) to report suspected adverse reactions to any of the medicinal products used in the treatment of these patients. This includes medicines administered to treat COVID-19, as well as those used in the management of long-term, pre-existing conditions. It also includes medicines that might be used off-label in the treatment of COVID-19.



Figure 1

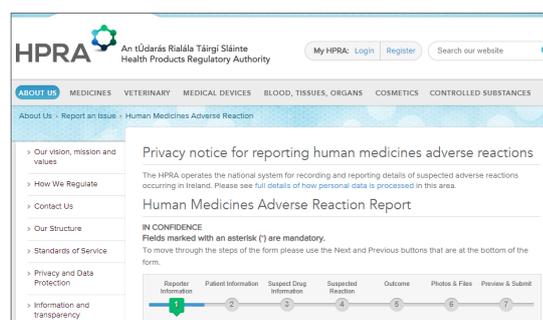


Figure 2 - HPRA online ADR reporting page

## Additional Monitoring

Healthcare professionals and patients are particularly encouraged and reminded to report all adverse reactions associated with the use of medicines subject to additional monitoring requirements, to support prompt identification of any new safety concerns associated with use. These medicines are identifiable by an inverted black triangle on the product information and an explanatory statement is included both in the Summary of Product Characteristics (SmPC) and Package Leaflet (PL) for these medicines, together with the symbol:

▼ This medicinal product is subject to additional monitoring

## Key messages

Information collected via adverse reaction reporting is an important method of monitoring medicines/vaccines safety in normal clinical practice.

As much information as possible should be provided on an ADR report form, however non-availability of all information should not deter reporting.

Suspected adverse reactions should be reported to the HPRa via the available methods ([www.hpra.ie/report](http://www.hpra.ie/report)).

Medicines subject to additional monitoring are identifiable by an inverted black triangle on their product information.

## Product information for medicines

The HPRa would like to remind healthcare professionals of the importance of regular review and monitoring of product information for medicines, to support awareness of relevant updates/changes which may affect prescribing, dispensing, administration or monitoring practices. Product information is regularly updated, following the assessment of new safety data, with, for example, several hundred recommendations to update product information made at EU level, following periodic safety reviews of medicines in 2019. It is also important that patients and care-givers, as appropriate, are made aware of the information contained in the Package Leaflet (PL) and should be encouraged to read it prior to and indeed during their treatment.

The product information is comprised of the Summary of Product Characteristics (SmPC) and the PL. These documents are issued when a medicine is first licensed for use and are reviewed and updated as necessary throughout the lifetime of a medicine, to reflect the current state of knowledge of the medicine and the risks associated with its use. The SmPC is mainly intended for use by healthcare professionals and SmPCs for medicines currently authorised in Ireland are accessible via the HPRa website ([www.hpra.ie](http://www.hpra.ie)) via the 'Find a Medicine' search function (see figure 3). The PL reflects the more comprehensive information described in the SmPC, but is required to be presented in an abbreviated and easy-to-read format for patients. PLs are also available on the HPRa website.

The SmPC provides the basis of information for healthcare professionals to use a medicine safely, effectively and in the most appropriate manner. It is also a legal document, agreed between the HPRa/EMA (European Medicines Agency) and the relevant pharmaceutical company. The format and content of the SmPC is laid down in EU/national legislation and regulatory guidance documents. Use of a medicine outside the conditions/recommendations described in the SmPC falls under the responsibility of the healthcare professional.

It is important to note that the SmPC is not intended to provide general advice on the treatment of particular medical conditions. On the other hand, specific aspects of the treatment related to use of the medicine, or its effects may be mentioned. Similarly, general advice on administration procedures is not included, but any advice specific to the medicine concerned will be included, if appropriate.

The PL is drawn up in accordance with the SmPC and is subject to user-testing to ensure its ease of readability by patients/consumers. It plays an essential part in supporting the safe and effective use of a medicine by a patient. Consequently, it is important that a PL is provided each time a product is dispensed. Patients and care-givers should be encouraged to read the current version of the PL that accompanies their medicine(s) and to discuss any relevant concerns with a healthcare professional involved in their care.

It is important to note that the product information for medicines authorised via the centralised application procedure, which is co-ordinated by the European Medicines Agency (EMA) and results in an authorisation which is valid across the EU, is available on the EMA website. The HPRa website provides a link to the EMA website via the SPC or PL link under the relevant medicine.

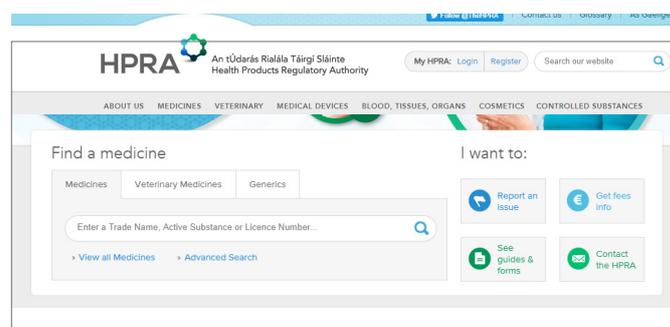


Figure 3 - HPRa 'Find a medicine' search function

Once on the EMA website ([www.ema.europa.eu](http://www.ema.europa.eu)), search the medicine name using the search box available (see figure 4), click on the relevant product and the product information is accessible from the 'Table of Contents'.

In specific situations where there is a need to take immediate action or change current practice in relation to a medicinal product, a direct healthcare professional communication (DHPC) is disseminated, prior to the product information change. A DHPC is a communication intervention by which important safety information is delivered directly to individual healthcare professionals by a marketing authorisation holder (MAH) following approval by the HPRA, to inform them of the need to take certain actions or adapt their practices in relation to a medicinal product. DHPCs deliver important safety information directly to HCPs. Situations when a DHPC may be disseminated include, for example, new major warnings or precautions for use in the product information, new data identifying a previously unknown risk or a change in the frequency/severity of a known risk, new recommendations for preventing or treating adverse reactions. A DHPC may also be used to inform of a suspension/withdrawal/revocation of a marketing authorisation for safety reasons. DHPCs are circulated by the MAH to HCPs by post as well as being published on the HPRA website under 'Latest updates' 'Safety notices' on the homepage. Please see article below on how to register with the HPRA for notification of safety alerts such as when DHPCs are published. In each edition of the HPRA Drug Safety Newsletter, a list with links to DHPCs published in the interval is provided.

Further initiatives are underway at a European level to facilitate access to product information and in January 2020, the EMA, the Heads of Medicines Agencies (HMA) of EU member states and the European Commission (EC) published [key principles](#) outlining a harmonised approach to develop and use of electronic product information (ePI) across the EU.



Figure 4 - Medicine search function on EMA website

## Key messages

Product information (SmPC and PL) is available for medicines currently authorised in Ireland from the HPRA/EMA websites (accessible from [www.hpra.ie](http://www.hpra.ie)).

The current versions of the product information should be consulted regularly to ensure medicines are used in the safest and most effective manner.

Patients should be encouraged to read the PLs provided with their medicines and to discuss any concerns with a relevant healthcare professional.

DHPCs circulated by MAHs are published and available on the HPRA website.

Access to electronic product information (ePI) is an initiative that was launched at European level to improve access to product information.

## Registering with the HPRA for safety alerts and updates

The HPRA website provides users with the option of registering their contact information with the HPRA to enable them to receive direct and immediate notification of alerts/updates by email. Users will be alerted to (depending on their recorded preferences) publications such as the HPRA Drug Safety Newsletter, Direct Healthcare Professional Communications (DHPCs) and alerts regarding new/updated safety/quality information on medicines/medical devices etc.

To facilitate prompt access to these updates, users are encouraged to avail of this option by registering on the website:

- Go to the HPRA webpage [www.hpra.ie](http://www.hpra.ie)
- Click on 'Register' in the 'My HPRA' box on the top right hand corner of the homepage
- Enter your details and click 'Register'
- You will be emailed a link to confirm registration to the email address nominated
- Once registration is confirmed, log in using your email address and password
- You will be brought to the 'My HPRA' page to manage your preferences
- Under 'My preferences', tick the stakeholder group (e.g. healthcare Professionals), topics of interest that you wish to receive updates about (e.g. safety and quality) and products of interest (Medicines).
- Please note that at any time you can log into My HPRA to update your preferences.

Correspondence/comments should be sent **by email only** to the Pharmacovigilance Section, Health Products Regulatory Authority, [medsafety@hpra.ie](mailto:medsafety@hpra.ie).