

A National Adverse Drug Reaction Reporting System for Malta

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Introduction

The mission of the Medicines Authority (MA) in Malta is to contribute to protection of public health through regulation of the safety, quality and efficacy of medicines for human use on the local market and to ensure that healthcare professionals and patients have access to accurate and up to date information about medicines. In order to disseminate information regarding safety of medicines, the MA publishes guidance notes for healthcare professionals and the pharmaceutical industry. The MA also publishes information on its website: <http://www.health.gov.mt/mru/>

On the 4th of May, 2004 the MA held a seminar to launch a national adverse drug reaction (ADR) reporting system involving the co-operation of doctors, dentists and pharmacists, as well as the pharmaceutical industry. The ADR reporting system will form part of an overall pharmacovigilance system within the Authority and this will be the primary means of collecting information useful in the surveillance of medicinal products.

Pharmacovigilance

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects of medicines and it is an important aspect of the regulation of medicines. The overall objectives of pharmacovigilance include early identification of potential safety hazards, evaluation, monitoring and where appropriate, implementation of regulatory action to maximise benefits and minimise risks associated with medicinal products. Notification and reporting of suspected ADRs arising with use of medicinal products, by healthcare professionals is an essential source of new information for the achievement of these objectives.

The need for drug safety monitoring

Not all hazards can be known before a medicinal product is marketed. Patients, consumers and indeed some healthcare professionals have expectations that medicinal products available are "safe" and may be surprised when regulatory action is taken to restrict their use, introduce new warning statements, or withdraw medicines as a result of new information regarding safety issues.

Information collected during the pre-marketing phase of a medicinal product is inevitably insufficient with regard to the complete safety profile of a product and animal testing is not necessarily predictive of human safety. Data from clinical trials is often limited by their size and duration and furthermore, conditions of use may differ during clinical trials from those encountered during normal clinical practice. Information about rare but serious adverse reactions, chronic toxicity, use in special groups (such as children, the elderly or pregnant women), or drug interactions is often incomplete or not available at all: this emphasises the need for ongoing surveillance.

All medicines have the potential to cause ADRs. It is estimated that ADRs cause admission to hospitals in as much as 2% to 6% of all cases. Furthermore, ADRs contribute to an increased attendance at primary health care level and may complicate hospital in-patient stay in as many as 10% to 20% of patients.¹ Moreover, ADRs may be responsible for deaths and they may possibly be the fourth commonest cause of death. They may increase the length of hospital stay and therefore increase the cost of patient care. In addition ADRs may adversely affect quality of life and may cause patients to lose confidence in doctors.¹

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ADRs also mimic disease and result in unnecessary investigations and possibly delay accurate diagnosis and treatment. As a corollary, occurrence of toxicity in a minority of patients might preclude use of an important medicinal product in the majority of patients, if predisposing factors cannot be identified and appropriate regulatory measures implemented to appropriately manage their risks.

Development of ADR reporting systems

Perhaps the greatest of all drug disasters was the thalidomide tragedy of 1961-1962, when thalidomide caused major birth defects in an estimated 10 000 children in the countries in which it was widely used for the treatment of nausea and vomiting in early pregnancy. The thalidomide disaster led to the establishment of drug regulation in many countries around the world. Such regulation requires that medicinal products are licensed by an established regulatory authority.²

The history of international pharmacovigilance goes back to when the Twentieth World Health Assembly adopted a resolution to start a project on the feasibility of an international system for monitoring adverse reactions to drugs. This resolution was the basis of the WHO Programme for International Drug Monitoring of 1968. Since then, many countries have established pharmacovigilance systems and there are now over 70 countries involved in the WHO Collaborating Programme for International Drug Monitoring.³ The establishment of a functional ADR reporting system not only facilitates participation in the national and EU regulatory process, but also enables Malta to participate in the WHO Programme for International Drug Monitoring, both by contributing to and obtaining data from this extensive information resource.

Legislation

The adverse drug reaction reporting system established in Malta is consistent with requirements established by European and Maltese legislation for the regulation of medicinal products. European legislation relating to the regulation of medicinal products for human use is embodied in Directive 2001/83/EC, recently revised and replaced by Directive 2004/27/EC. This Directive lays down requirements not only for persons marketing medicinal products in EU Member States but also for *competent authorities*. Competent Authorities in Member States, such as the Medicines Authority in Malta, 'shall establish a pharmacovigilance system – this system shall be used to collect information useful for the surveillance of medicinal products, with particular reference to adverse reactions in human beings and to evaluate such information scientifically.'⁴ Member States are also obliged to 'take all appropriate measures to encourage doctors and other healthcare professionals to report suspected adverse reactions to the competent authorities.'⁴

In addition, the competent authority of the Member State should 'suspend or revoke an authorization to place a medicinal product on the market where that product proves to be harmful in the normal conditions of use, or where therapeutic efficacy is lacking, or where qualitative and quantitative composition is not declared.'⁴

In November 2003, a new Medicines Act was published, replacing previous legislation. This Act established the regulatory framework for the Medicines Authority and further subsidiary legislation to the Medicines Act for pharmacovigilance was published in Legal Notice 22 of 2004. The Maltese pharmacovigilance regulations state that: 'It shall be the duty of doctors and other healthcare professionals to report to the Authority any suspected serious or unexpected adverse reaction to a medicinal product'.²

The role of health care professionals

In all countries, where pharmacovigilance systems operate, the role of healthcare professionals is vital in recording and reporting suspected ADRs observed in their practice, in order to alert regulatory agencies to new or emerging safety concerns, thus facilitating timely and appropriate regulatory action. The advantages of an ADR reporting system are:

- It is an inexpensive method of monitoring the safety of a medicinal product throughout its lifetime.
- Reports are based on unbiased observations made by vigilant healthcare professionals.
- It is an essential method of detecting signals of rare ADRs.
- It remains the primary method of data-collection used in most countries.

Participation of healthcare professionals is therefore essential for the effective functioning of a pharmacovigilance system and the reporting system introduced in Malta is a mandatory, country-wide system for the reporting of suspected ADRs.

How to report

For the purposes of reporting, an ADR reporting form has been designed and copies are available from the MA, and may be downloaded from <http://www.health.gov.mt/mru/> Receipt of any ADR forms sent to the MA will be acknowledged and the minimum information required for a valid report is:

- An identifiable reporter, (e.g. doctor, pharmacist, dentist)
- An identifiable patient (e.g. initials, age, sex)
- A suspected medicinal product
- A suspected ADR

Information contained in ADR reports will be entered on the MA's secure database and all personal data will be treated as confidential.

What to report

The legal obligation contained in Legal Notice 22 of 2004 and described previously, specifies the obligation for healthcare professionals to report to the Authority any suspected serious or unexpected ADR to a medicinal product. A *serious* ADR is one that is:

- Fatal
- Life threatening
- Causes or prolongs hospitalization
- Causes a congenital abnormality
- Causes disability or incapacity

An *unexpected* adverse drug reaction is one whose nature, severity or outcome is not consistent with the summary of product characteristics.⁴ However, healthcare professionals are also encouraged to report all suspected ADRs to the MA. In addition to data provided by healthcare professionals, pharmaceutical companies will also be obliged to provide pharmacovigilance data to the MA as a condition of their licence to market medicinal products.

Evaluation of data by the MA

ADR reports will be assessed in the context of other available data and MA staff will regularly review safety issues internally and with national experts and professional associations. In addition, MA staff will participate in scientific meetings that consider safety issues, such as the Pharmacovigilance Working Party of the Committee for Human Medicinal Products.

Implementation of regulatory action

As a result of the evaluation of pharmacovigilance data and in keeping with national and EU legislation, the MA may take regulatory action to vary, suspend or withdraw marketing authorisations for medicinal products, if considered appropriate.

Regulatory measures will be taken in order to prevent future serious ADRs, and to minimize the risks associated with use of medicinal products. When changes to product information are made to enhance safety, these will be communicated to healthcare professionals. Regular updates on important safety issues will be provided to healthcare professionals through a Newsletter issued by the MA, which will be published and distributed at regular intervals throughout the year. In urgent cases, specific letters would be sent to alert healthcare professionals of a new or emerging safety concern.

The MA will also have a role as an information service provider to healthcare professionals by making available the latest up-to-date drug safety information.

Conclusion

On-going monitoring of the safety of medicinal products is an essential component of pharmacovigilance and is a responsibility shared by healthcare professionals, the pharmaceutical industry and the MA, to ensure availability of complete, up-to-date safety information which in turn minimises individual patient risks.

The essential aim of legislation governing the production, distribution and use of medicinal products is to safeguard public health and EU legislation provides a framework that must be adopted by all member states. Implementation of EU and national legislation is without doubt a further step in ensuring availability of safe, efficacious and good quality medicinal products in Malta, in the interest of public health. The establishment of the MA as an EU competent authority, should contribute to improved patient care and safety and facilitate the overall assessment of medicinal products.

It is also hoped that establishment of the MA will enhance promotion of understanding and knowledge of healthcare professionals regarding safe use of medicinal products and provide an effective means of communication to both healthcare professionals and to the public.

Since the launch, the MA has already received and processed several suspected ADR reports and through such reporting, healthcare professionals make a positive contribution to the overall knowledge of the safety profile of medicines and to the national pharmacovigilance system.

References

1. Andrews E, Mann R, Pharmacovigilance. West Sussex: John Wiley & Sons. 2002; 1: 3-7.
2. Medicines Regulatory Unit. [Online]. 2004 [cited 2004 Jun 18]; Available from: <http://www.health.gov.mt/mru/>
3. Uppsala Monitoring Centre. World Health Organisation. [Online]. 2004 [cited 2004 Jun 18]; Available from: <http://www.who-umc.org/publ.html>
4. Eudralex. Directive 2001/83/EC. [Online]. 2004 [cited 2004 Jun 18]; Available from: <http://dg3.eudra.org/F2/eudralex/vol-1/home.htm>