Patient safety and pharmacovigilance

ABPI Pharmacovigilance Expert Network
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Introduction

Medicines may affect the body in unintended, harmful ways. These effects, called side effects, adverse events or adverse reactions, represent risks of medicines.

It is important to identify, as quickly as possible, new risks or changes to the known risks associated with the use of medicines. Actions must be taken to minimise the risks, maximise the benefits and promote safe and effective use of medicines by patients.

These activities are known as pharmacovigilance...

...The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem.

...An activity contributing to the protection of patients' and public health.

Additional information regarding the safety of medicines and pharmacovigilance can be found on the following websites:

Medicines and Healthcare products Regulatory Agency: Safety Information
www.mhra.gov.uk/safetyinformation/

European Medicines Agency: Human Regulatory – Pharmacovigilance
www.ema.europa.eu

European Commission: Public Health – Medicinal Products for Human Use – The EU Pharmacovigilance System
http://ec.europa.eu/health/human-use/pharmacovigilance

Definitions

Adverse Event (AE)
Any untoward medical occurrence in a patient or clinical trial subject administered a medicinal product, and which does not necessarily have a causal relationship with this treatment.

Adverse Drug Reaction (ADR)
A response to a medicinal product that is noxious and unintended. Response in this context means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility.

Other special safety situations
Safety data includes information about medicines used in the following situations: foetal exposure during pregnancy (via maternal or paternal drug use), neonatal exposure via breast feeding, overdose, abuse/misuse, medication errors, unapproved or off-label use (especially in paediatric or elderly populations), reports of lack of therapeutic effect or other product complaints, drug interactions, suspected transmission of infectious agents or occupational exposure.

Signal Detection
The review of individual safety reports to identify new or potentially new safety concerns or increases in the known risks associated with a medicine. It must be ensured that appropriate action is taken in response to new evidence that impacts on the known risk-benefit balance of a product (ie. a Risk Management System).

Risk Management System
A set of pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to a medicinal product, including the assessment of the effectiveness of those interventions.

Patient safety: everyone has a role

Healthcare professionals and the general public

The UK's national system for reporting safety information on medicinal products is the 'Yellow Card' Scheme (www.mhra.gov.uk/yellowcard), which is operated by the Medicines and Healthcare products Regulatory Agency (MHRA) and the Commission on Human Medicines (CHM). The scheme is used to collect information from both healthcare professionals (HCPs) and the general public on suspected adverse drug reactions (ADRs) to a medicine. Its continued success depends on the willingness of people to report suspected ADRs, as the scheme is voluntary.

HCPs in particular may have direct interactions with the pharmaceutical industry involving patient safety. For example, data on the incidence and management of ADRs may be requested from the company's medical information service to help manage a particular patient with that ADR; HCPs may participate in market research, post-marketing clinical studies or patient support programmes; HCPs may work with the company to give presentations on specific therapeutic areas, enhanced by patient case stories, which often involve tolerability issues.

There are many opportunities for such interactions and any time a patient is mentioned who has experienced an adverse event to the company's medicinal products; the company is obliged to collect data about the patient's experience.

Equally, assistance may be required to implement advice received on minimising risks to patients through updated product information, 'Dear HCP letter' or other materials, which are issued following agreement between pharmaceutical companies and the regulatory authorities.

Pharmaceutical companies

The company that holds the marketing authorisation (licence) for a medicine has mandatory legal obligations to continuously collect data about safety and adverse events reported in association with its products. The company must have rigorous systems in place to collect safety data from any activity it undertakes that involves the use of its medicines by patients. All employees and contractors within the company must be trained on these processes to ensure safety data is reported in a timely manner.

The company must collate and analyse the data to produce individual and cumulative safety reports and conduct pharmacovigilance activities such as signal detection and risk management.

Safety reports have to be transmitted to the regulatory authorities within defined timelines and any emerging concern about the benefit-risk balance of the product has to be notified immediately. If necessary, the authorities may request further investigations, including formal studies. Regulatory procedures exist for updating product information and implementing other safety measures.

Companies are subject to inspections by the authorities of their pharmacovigilance systems.

Regulatory authorities

Within Europe, pharmacovigilance activities are carried out collectively by the governmental regulatory authorities within the individual Member States, together with the European Commission and the European Medicines Agency (EMA).

Safety data from a variety of sources is received and reviewed. This includes data from individual patient experiences, results from clinical and epidemiological studies and published reports in the scientific literature etc. Data is received from pharmaceutical companies, academic units, individual HCPs or patients.

The EMA has established the Pharmacovigilance Risk Assessment Committee (PRAC), which meets once a month to provide recommendations on all aspects of pharmacovigilance, ranging from risk management and communications on the risks of adverse reactions, to the design and evaluation of post-licensing safety studies and pharmacovigilance audits.

Scientific networks are also developed by the authorities to improve the public health effectiveness of pharmacovigilance activities.

Patient safety and risk management

Once information on individual patient experiences of adverse events to a medicine have been collected from all the different sources, analysis of the data must take into account the following considerations:

- Case reports of suspected adverse reactions alone are rarely sufficient to confirm that a certain effect in a patient has been caused by a specific medicine.
- The fact that a suspected adverse reaction has been reported does not necessarily mean that the medicine has caused the observed effect, as this could have also been caused by the disease being treated, a new disease the patient developed, or by another medicine that the patient is taking. Case reports need, therefore, to be assessed by an expert.
- A single case report should be seen as a piece of a jigsaw puzzle, where further data are usually needed to complete the picture. These include data from worldwide spontaneous case reports, clinical trials and epidemiological studies.
- The number of case reports for a particular medicine or suspected adverse reaction does not only depend on the real frequency of the adverse reaction, but also on the extent and conditions of use of the medicine and the nature of the reaction as well as public awareness. Therefore, comparing numbers of case reports between medicines may give a misleading picture of their safety profiles.

Therefore, 'Risk Management Plans' have to be written to answer three key questions:

1. What is known or not known about the risks of the medicine?
2. What studies are needed to find out more about the risks?
3. What is needed to minimise the risks?

Risk management plans are updated throughout the life of the medicine, so over time the number of potential risks and missing information decreases. Risk minimisation can be about reducing the effects of the risk when it happens or reducing how often it happens.

Working together

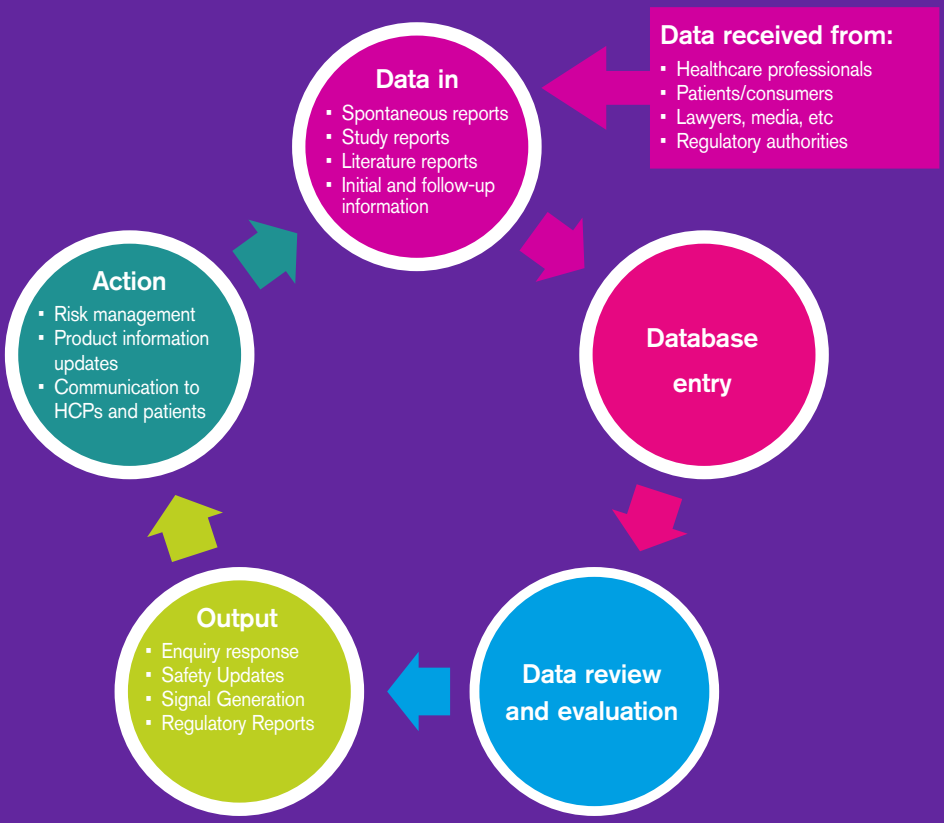
The pharmacovigilance process works most effectively when there is:

- appropriate exchange of safety data,
- sharing of resources,
- communication and transparency between all parties

This helps to ensure that patients, who are receiving medicinal treatments for the benefit of their health, can be protected from unnecessary risk.

http://www.ema.europa.eu/docs/en_GB/document_library/Report/2011/07/WC500109582.pdf

Overview of a company's pharmacovigilance process



By continuing to collect safety information on a medicine and taking action in response to the potential risks, the public can continue to be protected from emerging safety issues throughout a medicine's lifecycle.

ABPI

We represent innovative research-based biopharmaceutical companies, both large and small, leading an exciting new era of biosciences in the UK.

Our industry, a major contributor to the economy of the UK, brings life-saving and life-enhancing medicines to patients. Our members supply 90per cent of all medicines used by the NHS, and are researching anddeveloping over two-thirds of the current medicines pipeline, ensuring that the UK remains at the forefront of helping patients prevent and overcome diseases.

The ABPI is recognised by government as the industry body negotiating on behalf of the branded pharmaceutical industry, for statutory consultation requirements including the pricing scheme for medicines in the UK.

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