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The Role of the Pharmacist in Pharmacovigilance – A Regulatory Perspective

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Presentation Topics

- What is pharmacovigilance ?
- Development of pharmacovigilance systems
- Detecting adverse reactions
- Reporting suspected adverse reactions - how/when/why?
- Assessment of adverse reaction reports
- Regulatory Tools in Pharmacovigilance (Risk Minimisation Activities)
- The importance of pharmacovigilance



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Defining Pharmacovigilance

Pharmacovigilance

"The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or of any other drug-related problems"

WHO definition



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Pharmacovigilance

Being 'vigilant regarding medicines' is essential today because of:

- High usage of medicines
- Increasing complexity of medicines
- Polypharmacy
- Population growth and diversity

Adverse reactions to medicines constitute a major morbidity.



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CSD Assessment of Safety of Medicines

- No drug which is pharmacologically effective is entirely without hazard, the hazard may be insignificant or may be acceptable in relation to the drug's therapeutic action. Furthermore, not all hazards can be known before a drug is marketed: neither tests in animals or clinical trials in patients will always reveal all the possible side-effects of the drug. These may only be known when the drug has been administered to large numbers of patients over considerable periods of time."

Committee on Safety of Drugs (CSD) Report
(1966)



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Development of Regulatory & Pharmacovigilance Systems

- Post-thalidomide - US & European countries established formal monitoring systems

US - FDA, UK - MCA/MHRA

1966 - National Drugs Advisory Board (NDAB)

1995 - Irish Medicines Board

- 1995 - European Medicines Agency (EMA)
- 1968 - WHO Collaborating Programme for International Drug Monitoring



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Ideal Pharmacovigilance System

- Detect and assess signals rapidly and accurately
- Promote safe use of medicines
- Manage risks judiciously
- Communicate
- Engage all stakeholders



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Legal basis of Pharmacovigilance

- **Defined in national/EU legislation** – legal basis in the EU is given in Directive 2001/83/EC (as amended) and Regulation (EC) No 726/20042.

Includes requirements to:

- Encourage reporting of suspected adverse reactions & imposition of reporting requirements
- In consultation, to develop guidance on collection, verification and presentation of adverse reaction reports
- To exchange adverse reaction reports with pharmaceutical companies & the EMEA
- To monitor company compliance with pharmacovigilance obligations
- To take regulatory action if the view is taken that a product is harmful under normal conditions of use, lacks therapeutic efficacy, or if the risk/benefit balance is not positive under normal conditions of use, or if the qualitative/quantitative composition is not as declared



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International Collaboration & the IMB

- Commitment to EU systems for regulation of medicines
- Active participation in Scientific Committees and Working parties at EMEA level
- Established partnership in WHO programme for international drug monitoring (1968)



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Why do we need post-marketing surveillance?

Limitations of pre-marketing data

- Too few
- Too brief
- Too simple
- Too median - aged



Post-Marketing Monitoring

- "Real life use"
- Provides data from long term use and large patient groups
- Identifies occurrence of rare adverse reactions
- May help quantify incidence of established adverse reactions



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Reporting of Adverse Reactions by Healthcare Professionals

- Reporting system in place in Ireland since 1968
 - Doctors & Dentists
 - **Pharmacists (1980)**
 - Nurses (1986)
- Mandatory reporting requirements for pharmaceutical companies - condition of authorisation
- For the purposes of reporting suspected adverse reactions, Healthcare Professionals are defined as medically-qualified persons, such as physicians, dentists, pharmacists, nurses and coroners (EU guidance)



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Medication Risk Management System

An integrative approach to medication safety requires involvement of all stakeholders who include (among others):

- Pharmacist
 - Doctor
 - **Patient**
 - Company
 - Regulator
-
- Pharmacotherapy and pharmacovigilance should be integrated
 - Adverse reactions considered alongside indication, appropriate use, quality, patient participation, environmental impact.



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Reporting of Adverse Reactions by Pharmacists (1)

- Approximately 100-150 adverse reaction reports notified to the IMB by pharmacists each year (of a total of approx 2,000 nationally occurring cases)
- Significant opportunity for direct interaction
 - important educational roleObtain and provide information on:
 - long-term effects
 - drug interactions
 - OTC medicines, including herbal/homeopathic products



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What is an Adverse Reaction?

- A response to a medicinal product which is noxious and unintended and which occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease or for the restoration, correction or modification of physiological function

(EU & WHO definition)



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What is a Serious Adverse Reaction?

- A serious adverse reaction means an adverse reaction which results in death, is life-threatening, requires in-patient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or is a congenital anomaly/birth defect

(EU & WHO definition)



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Diagnosis of Adverse Drug Reactions

- Is the patient taking medicines? OTC, prescribed, herbal, oral contraceptives, misused drugs, long term prescription drugs.
- Medical history - right drug in the correct dose
- Patient's adherence to the prescription instructions

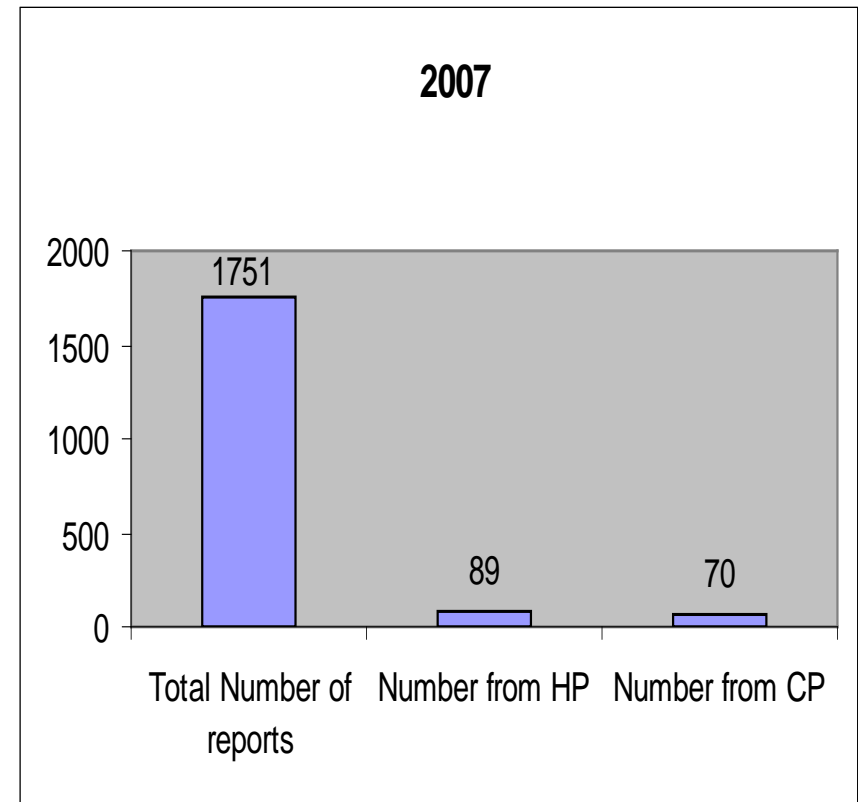
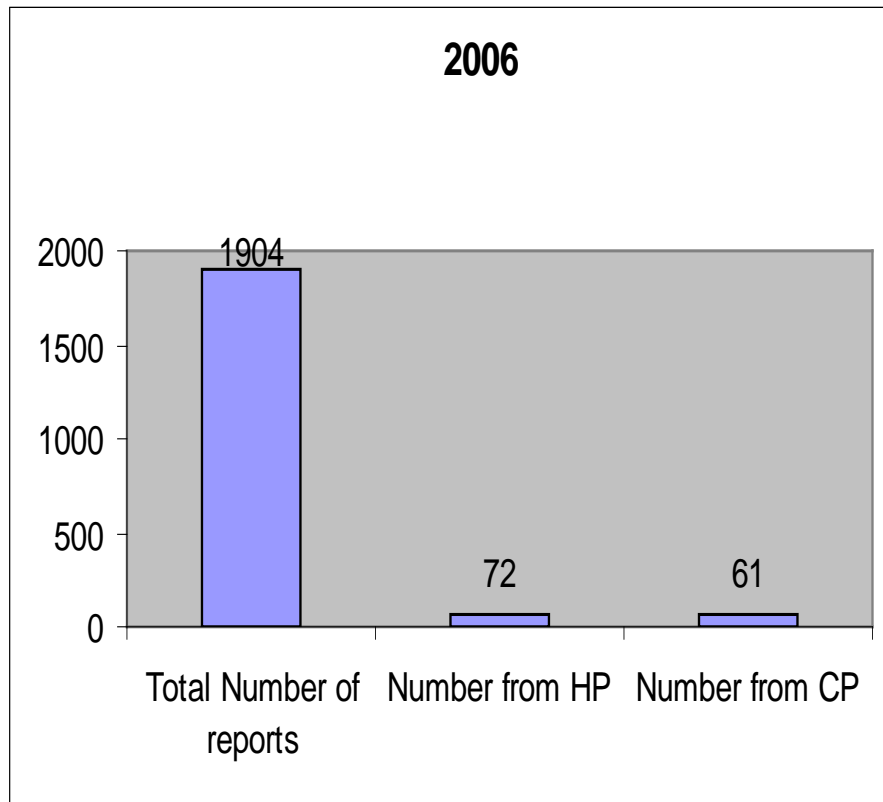


Diagnosis of Adverse Drug Reactions (2)

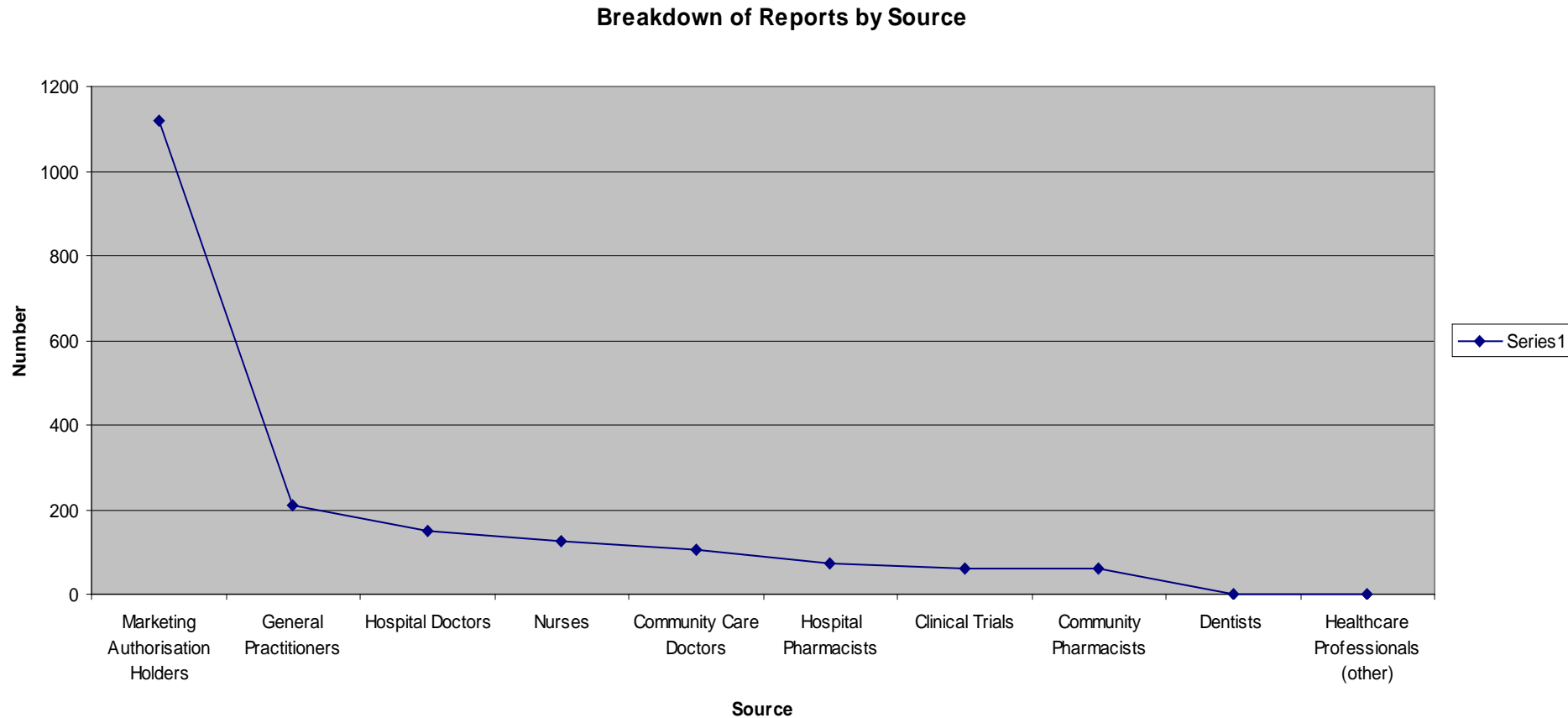
- Time relationship?
- Could it be a withdrawal reaction?
- Could this be an allergy?
- Is the patient pregnant?
- Consider known pharmacology
- Consider known idiosyncrasy
- Consider dose
- Consider interactions
- Consider risk/benefit for the particular patient



Reporting of Adverse Reactions by Pharmacists (2)



Overall Breakdown of Reports by Source - 2006



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Reporting responsibility

- Responsibility in professional field to be aware of and report adverse reactions
- Every report represents a patient concern
- Everything we do should ultimately benefit patient care



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Collecting and sharing information

- The quality of adverse reaction reports is critical
- Require ADR diagnosis as a basis for high quality reports
- Advancement in safety relies on reporting by healthcare professionals
- Report anything that is considered suspect
- Link pharmacovigilance to rationale use of medicines



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Reporting Suspected Adverse Reactions

What & When?

- Any suspected adverse reaction, but in particular
 - All suspected reactions to newly authorised medicines (i.e. those on the market for less than 2 years)
 - Serious, suspected reactions to established medicines
 - Any suspected increase in the frequency of non-serious reactions
 - Any suspected teratogenic effects
 - Any suspected reactions to vaccines

N.B. Emphasis on “suspected”



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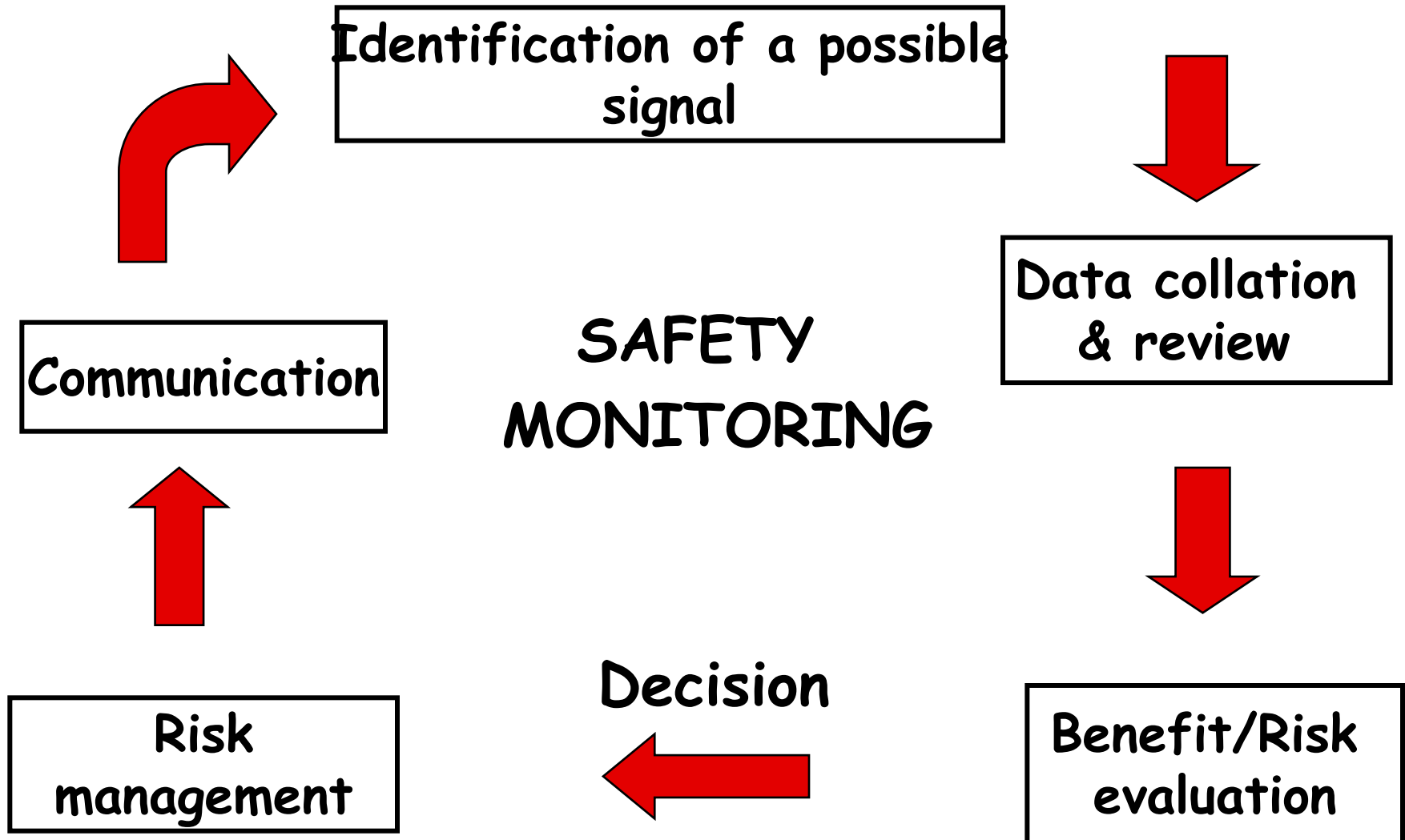
How to Report a Suspected Adverse Reaction

- Post-paid Report Cards (Yellow-Cards)
 - Available from website
 - On request from IMB (Tel: 01 6764971)
- IMB Website - <http://www.imb.ie>
 - Information on IMB activities
 - Drug Safety Newsletter & index of issues covered to date
 - **On-line & downloadable report forms**
 - Registration option - receive updates by text or e-mail.



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Evaluation of Pharmacovigilance Data



The Value of Adverse Reaction Reports

- Signal/hypothesis generation
- Facilitates review of other available data
 - international database sources
 - review of scientific literature
- Facilitates consideration of any need for epidemiological studies
- Permits revision of product information, +/- other regulatory action, as appropriate



Risk Minimisation Plan

Regulatory requirement to ensure pro-active product monitoring, based on existing knowledge and potential safety concerns

May need to be submitted:

- at any time of a product's life-cycle i.e. during pre-authorisation or post-authorisation phases
- on the initiative of Regulator/Marketing Authorisation Holder when safety concern identified.

Updated when:

- new information is received that may impact on the current safety specification, pharmacovigilance plan or risk minimisation activities - **spontaneous reporting helps to provide this new information** and allows identified risks to be addressed.



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Methods for Risk Minimisation

- Provision of information (SPC/PL)
- Educational Material
- Legal status of a medicine
- Control at pharmacy level
- Control of prescription size or validity
- Informed consent and other patient aspects
- Restricted Access Programmes
- Patient Registries



The Importance of Pharmacovigilance

- Patient/public health protection
- Effective early warning system
- Continuous surveillance over life-time of a medicine
- Facilitates risk identification and evaluation
- Communication of issues with safety implications
- Avoid drug “scares”
- Feedback information available
- Required by some journals



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CONCLUSION

- Pharmacovigilance is a shared activity/responsibility
- Relies on co-operation of all partners at local/national/international level
- Adverse reaction reporting is a vital component in safety monitoring
- Assessment of safety of medicines depends on the vigilance of healthcare professionals, prescribing, dispensing and monitoring use



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